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RESEARCH AND RESEARCH FINDINGS ON WOMEN'S HEALTH ISSUES

William F. Raub, Ph.D.
Deputy Director, NIH

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I. EXECUTIVE SUMMARY

In its report on the Fiscal Year 1991 budget for the Department of Health and Human Services (DHHS), the Senate Committee on Appropriations directed DHHS to publish a report (1) summarizing findings on women participants in the National Institute on Aging's Baltimore Longitudinal Study on Aging, (2) outlining research gaps concerning women's health and aging, and (3) recommending future research on aging issues of concern to women. The following report, as well as the attached annotated bibliography, has been prepared in response to this request.

Given the preponderance of women in the older age groups, the National Institute on Aging (NIA) has a particular interest in supporting research concerning the health and well-being of older women. NIA-supported research directly related to women's health issues includes studies of osteoporosis, especially as it relates to hip fractures: incontinence: hormonal changes with age: health-related behaviors: and the psychological well-being of women. Other NIA research addresses problems affecting both men and women.

The NIA Baltimore Longitudinal Study of Aging (BLSA), the central focus of this report, began in 1958. The women's cohort was established in 1978. There are currently 1,124 active BLSA participants (441 women and 683 men) who range in age from 20 to 97 years. The BLSA population is an open panel, and replacements are recruited when participants voluntarily withdraw or die. The goal is to maintain a sufficient number of participants to assure at least 30 women and 30 men in each age decade from the 20s to the 80s who have had a minimum of 12 years of observation (6 years of observation for participants who enroll in their 80s). Analyses of attrition are used to determine recruitment needs. Women currently account for about 40 percent of the study population and their rate of attrition (due to both death and dropout) is lower than that of male participants. There are over 100 BLSA publications reporting data based on women participants.

The BLSA has much to contribute to understanding and promoting women's health and well-being across the lifespan. BLSA participants are intensively studied for physiological and behavioral changes. Patterns of age changes are identified, mechanisms underlying the changes are elucidated, disease/aging interactions are evaluated, and normal standards as influenced by age are defined. Although there are similarities in age changes between men and women, many differences can be seen as well. Specific areas in which sex differences were found include: prevalence and presentation of certain diseases (urinary incontinence), rate of bone loss, immune function based on differences in the relative populations of various cells, a dramatic absence

of antibody to tetanus toxin in the serum of older women, patterns of body fat distribution and the ability to modify this distribution with weight loss, adequacy of nutritional intake, resistance to hearing loss, lower physical fitness levels, and aspects of memory function including immediate and delayed recall.

The absence of differences **between women and men is reflected in** an equally broad spectrum of areas. These include: forgetting of verbal material, relations of memory complaints to memory performance, utility of cardiac diagnostic tests in predicting silent myocardial ischemia, age related adaptations in cardiac structure and function, abdominal fat deposition among smokers, age-related deterioration of glucose tolerance, salivary gland output and other dental parameters, **equal** patterns of change in smoking habits and olfactory function, and stability of personality with age.

These results reflect the specificity, individuality, and complexity of sex differences and the aging processes. The next steps are further characterization and quantification of sex differences that remain to be identified as well as elucidation of their underlying mechanisms. Despite the conceptual and empirical gains won from the BLSA to date, a great many questions regarding women's health and aging remain to be answered.

There are inevitably more research opportunities available than can be actively pursued. Areas that would benefit from further study include: hormonal changes with age and the health implications of these changes; interventions and treatments that could alleviate or prevent **the** most serious manifestations of osteoporosis; frailty and disability in older women: cancer as it affects older women; preventive health behavior, and interventions that could motivate older women to use preventive health services; older women as givers and receivers of care; work and retirement patterns of older women: older minority women and older women in rural environments.

The NIA is planning or considering a variety of intramural and extramural research initiatives related to older women's health. These include testing osteoporosis prevention/intervention treatments, and related studies on the pathophysiology and mechanisms of osteoporosis; studies to address whether women are at greater risk for **Alzheimer's** disease than men: development of data bases on cancer in older people, including both men and **women: epidemiologic studies on health, functioning, and disability in older women, with special emphasis on minority women: and the role of** women as caregivers and how these are affected by socioeconomic circumstances. Current research interests also include the possibility of establishing a **special** population of peri-menopausal women as a complementary study to the BLSA. This initiative would allow the effects of the menopause (and possible interventions) to be studied longitudinally with a multidisciplinary approach, and would be pursued as resources permit.

II. INTRODUCTION

In its report on the Fiscal Year 1991 budget for the Department of Health and Human Services, the Senate Committee on Appropriations stated:

> ". . . One of the major sources for information on human aging, the Baltimore longitudinal studies on aging [BLSA], funded by the NIA, did not include women as subjects until 1978. As a consequence, the report issued by the Department of Health and Human Services, published in 1984, does not include any findings on women and aging or discuss the implications of gender on the aging process. Nevertheless, since 1978, more than 90 articles -- almost one-quarter of all publications -- on the BLSA have been published independently that include specific gender comparisons.
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> "The Committee directs the Department of Health and Human Services [HHS] to publish a report summarizing the findings on women based on data from the BLSA, the implications of gender on the aging process, the research gaps concerning women's health and aging, and recommendations for future research on aging issues of particular concern to women. The Committee requests that the report be submitted to Congress no later than March 1, 1991." (Senate Report No. 101-516, page 132)

The following report has been prepared by the National Institutes of Health of the Department of Health and Human Services in response to this request.

Women constitute approximately 59 percent of the United States population aged 65 and above, and about 72 percent of the population aged 85 and above. Given the preponderance of women in the older age groups, the National Institute on Aging (NIA) has a particular interest in supporting research concerning the health and well-being of older women, as well as predictors of later disability or frailty in this group.

The NIA supports both intramural research -- at the Gerontology Research Center in Baltimore, Maryland, and on the Bethesda campus -- and extramural research. The Baltimore Longitudinal Study of Aging is the NIA's major intramural study of human aging. The NIA also maintains a nationwide portfolio of grant-supported extramural research related to women's health issues. For example, the NIA supports an expanding program of osteoporosis-related research focusing on cause and progression of the disease, treatment and

prevention. Research on hormonal changes with age includes studies of the epidemiology of the menopause, regulation of gonadotropin secretion, and psychosocial aspects of menopause. NIA-supported research on incontinence focuses on prevention and management, addressing the special problems of women (such as complications resulting from long-term use of urinary catheters).

Current NIA-supported research directly related to women's health issues includes studies of osteoporosis, especially as it relates to hip fractures: incontinence: hormonal changes with age: health-related behaviors: and the psychological well-being of women. Other NIA research addresses problems affecting both men and women. Additional areas include Alzheimer's disease and other dementias, cancer, genetics, cardiovascular changes with age, nutrition, sensory dysfunction, immunology, frailty and its consequences, differentiation of normal versus pathological aging, and gender differences in social and behavioral factors associated with health and longevity.

Social and behavioral research on older women includes studies on self-care assessment and self-care behaviors; the effect of family and social support on health and quality of life; the psychosocial epidemiology of aging in middle-aged and older couples; and the roles of older women in the family and community. The NIA also supports both intramural and extramural longitudinal epidemiological studies to collect data on the health status of older men and women.

III. THE BALTIMORE LONGITUDINAL STUDY OF AGING (BLBA)

A. OVERVIEW

The Baltimore Longitudinal Study of Aging (BLSA) is the NIA's major intramural study of human aging. Since its beginnings in 1958, the BLSA has sought to understand how and why we age. The BLSA has evolved and changed over time, most significantly with the introduction of the women's cohort in 1978. The BLSA continues to be instrumental in dispelling myths about aging: in particular, that aging means a universal and inevitable decline in all physiologic and psychological functions. BLSA research demonstrates the complexity of aging processes in both women and men. Different organs, different systems, and, indeed, different individuals age at different rates. Recognition of this great diversity is essential to devising appropriate and effective interventions to increase the health, functioning, and well-being of older women. This report summarizes progress to date in realizing this potential.

1. BLSA Objectives

The overall scientific objectives of the BLSA are equally applicable to BLSA women and men. These are: (1) to identify differences among individuals of different ages and the changes that occur in these individuals with the passage of time; (2) to determine the relative contributions of aging, disease processes, birth-cohort effects and secular effects in producing observed differences and changes; (3) to establish the degree of interrelation and/or interaction among these factors; (4) to identify underlying mechanisms for observed age differences and changes; and (5) to expand scientific understanding about predictors and risk factors for specific diseases and for other end points related to successes and failures of adaptation to aging processes.

Further, comparisons of BLSA women and men are designed to provide insights into the still largely unexplained sex differences in, disease development and longevity. The major question being explored is how do differences between women and men -- including genetic, endocrine, and life style factors -- interact to cause (or prevent) disease and disability, to accentuate (or delay) the processes of aging, and to promote (or inhibit) longevity?

2. BLSA Methods

A variety of research methods -- longitudinal, cross-sectional, retrospective, and correlative -- are used appropriate to the

scientific questions being addressed. There are now over 50 BLSA studies in process, the majority of which are longitudinal in design. The longitudinal method is characterized by serial measurements of a specific variable on the same individual over time. It thus permits individual age changes to be identified. With the cross-sectional studies, average differences between age groups are identified at one point in time. Each method has its strengths and weaknesses, and the quantitative measurement of aging requires the application of both.

The BLSA incorporates distinctive features that collectively make it a unique resource for understanding how women age and for contributing significant new knowledge to the diagnosis and treatment of diseases and disabilities prevalent among older women. The study is woven into the fabric of the NIA intramural program. This allows a dynamic interchange of methods and ideas among experts in basic science and clinical medicine, fosters a multidisciplinary approach, and makes possible the conduct of clinical intervention studies in special cohorts. By its very nature, the BLSA is an observational study and has not employed interventions. The study design enables secular or environmental influences (changes in diet, alterations in physical activity, and smoking cessation) to be identified. By virtue of its wealth of measurements and characterization of participants' health history and current status, BLSA scientists are able to define age normative values for use in clinical practice. Finally, a variety of samples (blood, tissue, urine) is collected from participants at sequential visits and banked. As new assay techniques are developed, this bank together with the extensive health and behavioral data assembled over time on the participants allows an "instantaneous longitudinal study" to be conducted relating the new technique to risk factors and health outcomes.

Since 1986, an autopsy program has been in place. The objective is to enable post mortem and pathological findings to be related to functional assessment. Every consenting participant has been introduced to this program. At least 25% of the active participants have executed medical releases indicating that they expect their family to arrange to have an autopsy performed following death.

As of January 1, 1991, there were 472 men and 37 women deceased participants. Four hundred twenty-five (133 women and 292 men) have withdrawn or have had three or more years since their last visit. This latter group has been systematically contacted by telephone to re-enroll them either as active participants or as partially active participants to be followed periodically by telephone and mail communications. This was completed in March 1990. Another telephone followup is planned for 1992. Data from all three groups of participants -- active, inactive and deceased -- are used in various BLSA analyses and studies.

3. BLSA Participants

The study panel is a group of highly dedicated women and men who have volunteered to come to Baltimore every two years to be intensively studied to establish their physiological and psychological health and medical status. They now number 1,124 and range in age from 20 to 97 years. BLSA participants spend two and one-half days, and two nights on each visit undergoing a broad spectrum of tests and procedures. Certain of these are sophisticated, state-of-the-art diagnostic techniques **that make it possible** to detect occult disease in the absence of clinical signs or symptoms. Similar examinations and tests are administered to women and men: some are sex specific (pelvic and prostate examinations). **BLSA** men and women receive no remuneration for their participation and pay their own travel costs. Participants and their physicians receive a summary of the medical part of the evaluation and are advised of any problems of clinical significance.

Since 1978, 64% of first visit slots available to new participants have been assigned to women. As of January 1, 1991, there were 683 men and 441 women active participants. BLSA participants are enrolled in the study for as long as possible, and considerable efforts are made to keep participants from becoming inactive.

The BLSA population is an open panel. When participants voluntarily withdraw or die, replacements are recruited from a waiting list. The total size of the study group varies somewhat from year to year. The goal is to maintain a sufficient number of participants to assure that at any point in time there will be at least 30 women and 30 men in each age decade from the 20s to the 80s who have had a minimum of 12 years of observation -- 6 years of observation for participants entering in their 80s. The number of participants who can be evaluated in ***one*** year is a function of staff and space. Assuring the continuing availability of at least 30 men and 30 women in their 80s who have been followed at least 12 years is precluded at this time by the high losses in this age group and available resources. This population structure allows new studies -- based on research advances, novel ideas or the availability of new techniques -- to be initiated with the assurance that longitudinal follow-up of adequate numbers of women and men in each age decade will be possible.

To meet this population goal, analyses of attrition are used as a basis for estimating the number of recruits needed. Since losses (death and voluntary withdrawal) are higher at older ages and among men than women, more old than young participants and more men than women are enrolled. This population structure is designed to ensure that analyses of BLSA data on women and men can be made with equal levels of confidence.

The education, occupation and marriage of BLSA men and women entering the study since 1978 have been compared. Over 60% of women and men possess a bachelor's degree or higher. Although more men than women had earned advanced degrees, the percentages are similar in the 18-39 age group. Over 80% of men worked in professional, technical or management careers compared to 64% of women: again, there were no sex differences in the 18-39 age group. Over 80% of men were married at either the first or last visit, as compared to 71% of the women. Never married women (11%) exceed never married men (2%) in the 65-84 year age group. Both the differences in characteristics in marriage and employment between the younger and older women and the comparability in education and occupational characteristics between men and women in the 18-39 age group reflect temporal societal changes in the role of women. Understanding how these changes may affect women's health over the long term is a BLSA objective.

B. RESEARCH FINDINGS RELEVANT TO WOMEN'S HEALTH

Research results derived from ongoing and completed studies of BLSA women are described below. Areas where sex differences have emerged or earlier findings in men have been replicated in the women's cohort are highlighted. Future plans to augment the scientific data base assembled on BLSA women are briefly sketched, and selected research opportunities to contribute new knowledge relevant to women's health and well-being are identified. In addition, selected clinical research directly relevant to women's health (incontinence, postmenopausal hormone replacement therapy) conducted on special populations is briefly described. The Appendix to this report contains an annotated bibliography of the research summarized below.

1. Postmenopausal Hormone Replacement Therapy

Women in modern society spend about one-third of their lifespan in the postmenopausal state. The adverse effects of deficient secretion of the ovarian sex hormones, estrogens and progesterone, after the menopause include: (1) acceleration of bone loss leading to osteoporosis and increased risk of fracture; (2) an increased risk of coronary heart disease due in part to changes in cholesterol and other factors; and (3) symptoms such as urinary incontinence, hot flashes, and sexual difficulties. The efficacy of estrogen replacement therapy in preventing long term bone loss and treating female hormone deficiency symptoms has been demonstrated. Its beneficial effects on blood cholesterol and possibly cardiac risk may be as important as its effects on bone because coronary disease is still the number one cause of death in postmenopausal women.

Several questions regarding postmenopausal hormone replacement therapy remain unresolved. These include: (1) what are the best type, route, dose, and timing of estrogen and progestin treatment

to maximize benefits and minimize risks: (2) how are the effects of estrogens and progestins influenced by age and body type (both amount and distribution of body fat are influenced by sex hormones and contribute to risks of high blood pressure, diabetes, and heart disease); and (3) what are the mechanisms of estrogen and progestin action on bone and how do they interact with growth hormone and local growth factors. Growth factors play a key role in maintenance of bone and muscle tissue and tend to decrease in the elderly; their r&lease and action are affected by sex hormones.

Research by BLSA investigators to address these questions has focused on a newer form of estrogen treatment that is given through the skin, and may have advantages over pills. Studies have examined whether the effects of estrogen are: (1) different in younger versus older women; (2) modified by the addition of progestin, and (3) whether estrogen-progestin therapy might be working indirectly by inducing release of growth hormone or growth factors. (These studies were conducted with a specially recruited group of women rather than BLSA participants as the research design required diagnostic and therapeutic intervention.) The results demonstrate that: (1) clinical and biochemical beneficial effects and side-effects are similar in younger and older (over age 60) women: (2) addition of progestin does not alter estrogen effects in either age group; and (3) the provocative finding that transdermal estrogen inhibits growth hormone secretion whereas conventional oral estrogen treatment stimulates it.

To elucidate the basis for these results, current and planned future research in supplemental study cohorts will compare benefits and adverse effects of different forms of oral versus transdermal hormone replacement therapy in older versus younger postmenopausal women. In addition it will examine the separate and interactive effects of age, the amount and distribution of body fat, sex steroids, and growth hormone and related growth factors on bone structure and function, muscle strength, and glucose and lipid homeostasis; and the responses of these bone, muscle and metabolic parameters to administration of estrogens, progestins, and/or various growth factors.

2. Health and Disease Status of BLSA Women

A comprehensive clinical evaluation is conducted on each BLSA participant on each visit. A major new emphasis is being given to use of the clinical evaluation data base to compare major health differences between BLSA men and women. Results include:

Coronary Heart Disease and Hypertension -- Women are known to develop coronary heart disease (CHD) and hypertension (HTN) at a later age than men. Preliminary findings show the prevalence of HTN in women, until the menopause, was lower than in men. Treatment patterns were similar once HTN was diagnosed. On the other hand, the prevalence of diagnosed CHD remained lower in BLSA women

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at all ages. More women with CHD had a clinical diagnosis of angina (65%) than men (44%), while men had more myocardial infarctions. Treatment for CHD appeared to show that women received medication following diagnosis later than men, but, once treated, the number and types of medications were similar. BLSA men were more likely to have surgical procedures to correct the damage to their coronary blood supply.

These preliminary findings argue that the development of hypertension and coronary heart disease differ by sex. The clinical presentation of these diseases and their subsequent treatment may differ as well. The planned longitudinal observation of these women is critical to understand the significance of these sex differences.

Health Factors in Postmenopausal Women -- Clinical data on BLSA postmenopausal women are being reviewed to examine possible associations among type of menopause and estrogen usage with specific risk factors, mortality and disease. Of 279 postmenopausal women, 69 percent had natural menopause: 31 percent had artificial (i.e. surgically induced) menopause. Approximately 57 percent have had estrogen replacement therapy at some time. Of these, 55 percent are currently on replacement therapy.

Stress Incontinence in BLSA Women -- Estimates of the prevalence of urinary incontinence in the general population show a sex difference -- 18% in men and 22-39% in women. A study of the prevalence of self-reported urinary incontinence (SUI) in the BLSA population indicated a significantly greater sex differential. The prevalence in BLSA men (18%) was comparable to national samples. However, over 50% of BLSA women have reported SUI on at least one visit: and of BLSA women with multiple visits to the study who had SUI, 53% report it at every visit. Up to 45% of women with SUI report that it is intermittent, and 35% experience a remission. The extent and pattern of SUI in these BLSA women suggests a physiological deficit in the tissues controlling urination. Behavioral training methods have shown a high success rate in improving bladder control, and a number of BLSA participants suffering from incontinence have, on an individual basis, availed themselves of the behavioral treatments described below.

3. Behavioral Treatments for Incontinence in Women

There are more than two million community-dwelling adults in this country who suffer from urinary incontinence. Twice as many women as men are at risk. Approximately 50% of nursing home residents are incontinent. NIA intramural researchers have developed behavioral principles and techniques to treat incontinence which are now widely used in clinical practice. This research has involved special populations rather than BLSA participants. Based on clinical studies of 90 patients (77 women), use of behavioral training methods resulted in approximately an 80% improvement in

bladder function. A study of 18 elderly patients, 15 of whom were women, indicates that age is not a limiting factor for therapy. These studies have been extended into the nursing home setting. An evaluation of 39 female and 23 male nursing home residents. demonstrated that by using a combination of behavioral treatments and staff management procedures, it was possible to reduce the prevalence of incontinence by about 1 episode per patient per day: this outcome, applied on a national basis, could yield impressive cost savings.

4. Cognitive Aging and Alzheimer's Disease

Women's Coanitive Aaing -- In general, BLSA longitudinal research shows that only gradual and modest changes in various aspects of cognitive performance occur in women with aging. Most aspects of women's verbal intelligence and semantic memory do not show any significant changes with age. Marked or precipitous declines in these aspects of cognitive functioning are harbingers of pathological conditions and should be evaluated. Other recent findings show that women respond comparably to men in terms of ability to detect infrequently occurring targets: women forgot sentences at rates that were identical to those of men, but older men and women recalled fewer sentences after 24 hours than young men and women. Women are significantly better at immediate and delayed verbal recall whereas men are significantly better in immediate recall of digits.

Meta-Memory and Memory Performance in Women -- Although considered a hallmark of neurodegenerative diseases, memory complaints (in the absence of neurological evidence of impairment) were not predictive of poorer neurological test performance by BLSA participants. Instead, such complaints are associated with characteristic tendencies toward somatic complaining and psychological distress in both men and women. Women were no more likely to complain about declines in their memory than were men. The implications for research and clinical practice are that memory complaints themselves are probably not useful as a screen for early signs of dementia. BLSA longitudinal studies in this area reinforce the necessity for prospective studies of dementia using state-of-the-art neuropsychological evaluations.

Coanitive Status and Alzheimer's Disease -- A primary objective of BLSA research on cognition in normal aging concerns detection. of early signs of Alzheimer's disease via a prospective study of the natural history of dementia in the BLSA. A comprehensive battery of cognitive and neuropsychological tests is administered to BLSA men and women over age 60 to detect early signs of cognitive decline. This study seeks to capitalize on BLSA archival data. Impairments in memory and other cognitive processes that usually do not decline with aging may be promising predictors of cognitive decline and/or brain disease. Deficits in the ability to immediately recall and immediately recognize material were shown

to be important and independent indicators of mental status in both women and men. Ongoing BLSA research will explore the implications of these findings for the neuropsychological assessment and diagnosis of cognitive aging and brain disease.

A multifaceted NIA research program is underway at the Clinical Center on the NIH campus on Alzheimer's disease and other dementias. Special cohorts of women are enrolled in these studies which use an array of sophisticated brain imaging techniques. To date, women have not shown any differences from men with regard to any measure that characterizes Alzheimer's disease.

5. Osteoporosis and Age Related Bone Loss

BLSA studies on age related changes in bone metabolism are one component of an integrated basic and clinical initiative on osteoporosis which is exploring novel methods to sustain or stimulate bone formation.

Bone density studies demonstrated that premenopausal women showed no decreased bone with age at any of the four sites evaluated (small bones of the hand, forearm, lumbar spine, and hip). In older postmenopausal women (60 years and older), bone at each site was lost and at a faster rate compared to the loss of bone by men of the same age. Age and sex differences in certain vitamins, minerals, and hormones thought to play a role in the modulation and control of bone metabolism were evaluated. There were no significant changes in levels of vitamin D or its active metabolite with age in either sex. However, parathyroid hormone (PTH) levels increased and kidney function decreased with age in both men and women. Serum calcium values remained stable in women and declined slightly in men. Other changes in the bone regulating parameters measured did not differ between men and women with the exception of serum phosphorus levels, which were stable in women but declined in men. However, different patterns of bone turnover were observed: bone loss in older women was correlated with measures of high bone turnover, while this correlation was not shown in older men. Finally, there was no relationship of age-adjusted performance on tests of physical fitness and bone mineral density; those individuals of any age who were the most fit were not necessarily the ones who had the best bone.

A group of BLSA women and men with low bone mineral density status has now been identified. Longitudinal reexamination will enable a subset of these individuals to be identified as "fast losers". Such a group represents an ideal cohort to study new markers for bone status (collagen byproducts) and possible interventions (anti-resorptive drugs).

6. Silent Myocardial Ischemia

It is not known whether an abnormal exercise test response has similar predictive ability for subsequent coronary events (angina, heart attack, or sudden cardiac death) in both sexes. To address this question, maximal treadmill exercise testing of 726 apparently healthy BLSA women and men was conducted. An abnormal ECC exercise response increased the risk of a future coronary event nearly threefold in both sexes. This increase in risk was similar whether the first exercise test was abnormal or whether the individual converted from a normal initial response to an abnormal response on a later BLSA visit. To determine whether the addition of thallium heart scans aftermaximumtreadmillexercise would improve the ability to predict future coronary events over conventional exercise ECG alone, thallium scans on 407 apparently healthy BLSA volunteers were performed. The combination of an abnormal exercise ECG with an abnormal thallium scan predicted a 3.6-fold risk of coronary events over the subsequent five years, independent of conventional risk factors such as age, gender or hypertension. Women were less likely than men to show this combination of exercise ECG and thallium abnormalities. However, the serious implications of these abnormalities, when present, are similar for both women and men. These results suggest that such combination testing should be further investigated as a potentially useful diagnostic strategy in individuals with additional coronary risk factors.

7. Immune Function and Susceptibility to Infectious Disease

With increasing age there is a decline in immune function that is responsible for an increase in the number and severity of infections, a loss of ability to inhibit tumor growth, and an increase in the appearance of abnormal antibodies that react against one's own body (autoantibodies). The age related defect in immune function is due to a loss of cellular control mechanisms, but the mechanisms responsible are not presently known. The types of immune cells in the circulation of BLSA women and men are being examined to elucidate the factors responsible for control of immune function. Significant age and sex differences have been revealed which vary by cell type, as follows:

B cells are responsible for the synthesis of antibodies. The population (relative numbers) of early immature B cells in the blood are more common in older women than in older men, and decrease in men with age while increasing in women. The cells which control these B cells, the inhibitory and promotor T cells, show an age related decline in representation in both women and men. However, the enumeration of promotor T cells that provide a memory function (allowing a quicker immune response to a pathogen) shows an age related increase which is much greater in men than women. The increase in this cell population is at the expense of the T cell group that are uncommitted (available to respond to a

pathogen encountered for the first time). There is an age related loss of these cells in men and women, but the loss is much greater in men. There is no loss of Natural Killer (NK) cells, which have the ability to kill tumor cells, or NK activity with age in either women or men, but there is significantly lower NK cell representation and NK cell activity in young adult women compared to young adult men. Further, the amount of antibody to tetanus toxoid declines with age in both BLSA men and women. However, this decline is much steeper in women: virtually no women over age 55 have antibody to the Toxoid in their serum, placing them at much higher risk of developing tetanus and suggesting current immunization practices should be rethought for older women.

Collectively, these findings suggest: young women would be more susceptible to tumor growth than young men: older women can respond to new antigens better than old men: old men maintain immunologic memory better than old women: and old women would be more prone to produce autoantibody. Further research is needed to determine the basis for the observed sex differences and to test these hypotheses. If confirmed, they suggest that vaccines may need to be customized for women to ensure maximum efficacy.

8. Cardiac Structure and Resting Function

From past studies in elderly patients with high blood pressure has come the perception that elderly women have smaller, thicker hearts than elderly men. Echocardiogram and radioisotope studies on healthy BLSA volunteers, more representative of the general population, demonstrated that elderly women and elderly men have hearts of similar thickness. In both sexes, there is an age-associated increase in heart wall thickness which may be related to the rise in blood pressure that occurs with advancing age. As a consequence of its thicker and therefore stiffer walls, the older heart in both women and men fills with blood more slowly than its younger counterpart. This slower early filling rate with age is offset by greater filling late in the heart cycle, caused by the heart's upper chambers or atria. Thus, while there are definite structural and functional changes with age, there is no distinctive profile for the elderly woman's heart.

9. Physical Fitness in Women

Maximal oxygen consumption (VO_2max), the best measure of physical fitness, has been shown to decline between 5-10% per decade in men. Although women on average are known to have lower physical fitness levels than men, the reason for this sex difference is unclear. To address this issue, VO_2max was measured during treadmill exercise in healthy BLSA volunteers. In this BLSA study, men had approximately a 20% higher VO_2max than women at any age. During strenuous aerobic exercise, over 90% of the oxygen is consumed by the exercising muscles, the mass of which is smaller in women than men. To see whether this sex difference in muscle mass might help

explain the lower VO_2max in women, VO_2max was normalized to the total muscle mass rather than to the traditional variable, total body weight. When VO_2max was expressed in this manner, the gender difference in VO_2max was abolished. This suggests that women's smaller muscle mass may be the major factor in their lower maximal aerobic capacity.

Data from BLSA physical activity histories, a special physical activity supplemental questionnaire, and objective physical activity monitoring during participants' biennial visits are being analyzed. A study of self-reported physical activity of all BLSA men and women (ages 19-94) indicates that questionnaires for older adults should target activities of daily living, low and moderate intensity sports and leisure activities. This study showed that energy expenditure declines significantly with age, especially in high and moderate intensity activities. With increasing age, the primary sources of energy expenditure for both men and women are walking and housework. These data suggest that intervention studies to alter exercise habits and physical activity levels in older adults should be designed and pursued.

10. Body Fat Distribution, Gender and Longevity

Women have about 50% more body fat than men at all adult ages, yet they have a much more favorable morbidity and mortality experience. Capitalizing on the extensive BLSA data base, including repeated measures of body composition and biochemical tests of metabolic function, BLSA scientists conclude that at least part of the explanation for women's more favorable morbidity and mortality experience lies in sex differences in body fat distribution patterns.

Comprehensive data are now available from the BLSA on the pattern of distribution of body fat in women and men across the entire adult age spectrum. The sites of fat deposit differ markedly among women and men, and the pattern of distribution is now known to be as important as the quantity of fat stored in the body. The important characteristic in terms of health variables is the relative amount of fat deposited in the abdominal area compared, for example, to the hip-buttocks-thigh area. This pattern can be expressed as the ratio of the waist circumference to the hip circumference (WHR). A high WHR has been shown to be highly correlated with high cholesterol and triglyceride plasma levels, with abnormal glucose metabolism, and with elevation of blood pressure. In a predictive sense, a high WHR correlates with mortality itself. The WHR is much higher in men than in women and increases progressively with age. In men, the predominant increase occurs from the early adult to the middle-aged years. In contrast, in women, the surge in WHR occurs post-menopausally; but, at all ages, women have a much more favorable fat distribution than men. Current concepts suggest that lipid released from abdominal stores affects the liver with resultant overproduction of dangerous plasma lipids and with

elevation of circulating insulin levels. At present, the mechanisms underlying the sex differences in fat distribution are uncertain, but presumably are genetic and hormonal in nature.

The longitudinal character of the BLSA has enabled the effects of changes in body weight as time passes on the fat pattern to be examined. Sex differences are striking in this respect: in men, weight loss leads to a definite change in the WHR toward more healthful levels: in contrast, in women the fat pattern is quite resistant to change. Among the lifestyle variables that influence the pattern of body fat is cigarette smoking. BLSA research shows that, in both male and female cigarette smokers, fat is preferentially deposited in the abdominal area. Women, who use weight control as their reason for continuing to smoke, are striking a bad bargain: their weights will be affected trivially, and they will add a worsening fat pattern to all of the other well-known hazards of cigarette smoking.

In a related study, the effect of such lifestyle variables as fatness and fitness on the tendency to develop diabetes, as measured by the glucose tolerance test, was examined. The BLSA men and women both showed a progressive decline in physical fitness with increasing age: fitness in women was at a considerably lower level than that in men at all ages. Women were also much fatter than men but had a much better fat distribution pattern. In general, the women had a more favorable glucose tolerance than men despite their greater fatness and poor fitness. The increasing tendency toward diabetes with increasing age is indeed largely explained in both sexes by these lifestyle variables in the middle-age years. In old age, however, a deterioration of glucose tolerance occurs quite independent of increasing fatness and decreasing fitness. In this respect, the changes in glucose metabolism are quite similar in men and women.

11. Nutrition

Results of an evaluation of dietary intake and vitamin supplement use by age and sex indicate that women are at greater risk of marginal intakes for some nutrients than men. Even in the well-nourished, health-conscious BLSA population, diet alone does not provide adequate (greater than two/thirds of the recommended dietary allowance) amounts of iron for young women: calcium for women of all ages: and vitamin B_6, magnesium, and zinc for substantial numbers of both men and women. However, more women than men take vitamin supplements. Mean cholesterol intakes of women of all age groups was less than the 300 mg maximum recommended by the National Academy of Sciences; while cholesterol intakes of men averaged about 375 mg/day. Fiber intake was higher and fat intake lower in older men and women than in younger counterparts.

Antioxidant vitamins (A,C,E) have been reported to protect against a number of conditions associated with aging. Biochemical tests

of the circulating blood levels of these vitamins have revealed age and sex differences. For example, plasma vitamin C levels were higher in women than in men and were higher in older people. One suggestive finding to date is that BLSA participants with higher plasma vitamin C levels also had high levels of **HDL2-cholesterol. HDL2-cholesterol** is considered to play an important role in protection against cardiovascular disease. Collaborative studies on B vitamins and memory loss with Tufts USDA Human Nutrition Center on Aging recently began. A number of analyses to examine the effects of antioxidant vitamins on heart disease, immune function, pulmonary function, and development of various cancers in both men and women are planned.

12. Pulmonary Function

Pulmonary function as measuredby forced expiratory volume declines with age in men and women. The age effect is exaggerated by smoking and disease: although the effects of smoking are partly reversible. BLSA studies show that low levels of pulmonary function, supposedly within normal limits, were associated with earlier mortality. More extended studies indicate that the **age-**related decline in pulmonary function is a constant, thus allowing predictive declines. Deviations from this regular decline are observed in some individuals and appear to predict morbidity. In particular, recently completed longitudinal analyses indicate that deviations predict the development of ischemic heart disease in **BLSA** men. Analyses of the women's data are underway.

Part of the decline in pulmonary function may be attributable to a decline in muscle strength. An auxiliary study of opera singers shows that their age difference in pulmonary function is smaller than observed in BLSA participants. One difference between opera singers and most of the population is their training in **diaphragmatic** breathing which can effect pulmonary function. To explore the possibility that the age related decline in pulmonary function can be modified, a-special study on training persons in **diaphragmatic** training is planned.

13. Women's Oral Health

The following studies have been done in collaboration with the National Institute of Dental Research:

Salivary Gland Function -- Both BLSA cross-sectional studies and **recent ten** year longitudinal results indicate that in healthy women and men, salivary gland output is age-independent. No sex differences were found. Studies on electrolyte and antimicrobial protein concentrations in saliva from healthy women and men have shown essentially no age-related differences. Traditionally, complaints of burning tongue and mouth, and salivary gland dysfunction, have been attributed to the menopause. A BLSA study found no differences of oral complaints or salivary gland function

between premenopausal and postmenopausal women.

Dental, Periodontal, and Mucosal Disease -- There is a higher prevalence of dental disease with increased age in both BLSA women and men. Gingival disease appeared to be age stable among both sexes, although periodontal disease indices showed an increased amount of attachment loss among older individuals. Results of a study of oral mucosal function suggest that chronologic age per se does not predict the presence of overt oral mucosal alterations. The only age/sex group with an increase in mucosal alterations were older females wearing removable prostheses who did not remove their appliances during sleeping hours.

Oral Motor Function -- An increased prevalence of altered motor performance with age was found for parameters measuring lip tone and masticatory muscle function in both women and men. No age changes were detected in tongue function and swallowing in women. The temporomandibular joint (TMJ) is the focus of a variety of craniofacial pain disorders. The majority of reports profiling TMJ patients suggest that 80% are women. Contrary to certain other reports that various components of this joint undergo degenerative alterations with increased age, BLSA research does not confirm TMJ functional impairment as a "normal" age-associated event. Limitation of jaw opening among older BLSA women and men was the only age difference noted.

Dental impressions of participants are being examined by scanning electron microscopy to provide baseline data for subsequent calculations of rates and patterns of tooth wear and changes over time. A study of diabetes and glucose metabolism in conjunction with aging and oral health is underway: future studies are planned to assess the effects of other systemic diseases and their treatment upon aging oral physiology.

14. Smoking

Analysis of BLSA data reveal striking declines over time in the prevalence of cigarette smoking among both men and women. The trends from 1978 to 1990 are generally similar for men and women with the prevalence declining from over 30% to 20% among 20-39 year olds, remaining steady at approximately 20% among 40-59 year olds, and declining from 15% to 7% among 60-79 year olds. Although the prevalence of smoking was dropping over time, male and female smokers were starting smoking at progressively earlier ages over this same time period. These BLSA trends in smoking prevalence and starting age complement similar observations from large-scale epidemiologic studies. How this significant change in health behavior will effect morbidity and mortality in the BLSA population is part of the future BLSA research agenda.

15. Sex Differences in Brain Metabolism and Structure

The NIA intramural program also conducts a longitudinal study of brain structure and function in healthy men and women and compares age changes with those observed in disease states such as **Alzheimer's** disease. The methods employed include positron emission tomography (PET) to measure brain glucose metabolism; computer assisted tomography (CT) and magnetic resonance imaging (MRI) to measure brain anatomy: and neuropsychological tests to measure cognitive function.

Brain Metabolism -- PET was used to measure resting regional cerebral glucose utilization in women and men. A comparison of healthy young women and men showed no significant differences in absolute global or regional glucose metabolism, although more subtle differences in brain metabolism do exist. A new correlation method, developed by NIA intramural scientists, was used to look at interrelations between pairs of metabolic rates in different brain regions of healthy men and women, **18-40** years old, who were scanned under conditions of reduced auditory and visual stimulation. The results showed that women have more correlated brain activity in the left hemisphere than men. It is likely that this difference reflects a greater language ability in women than men. The relation of brain metabolism to age in both men and women is now being examined. Initial results indicate distinct differences in relation to age between men and women, with regard to metabolic correlations, but no distinct difference with regard to average metabolic rates.

Brain Anatomy -- To examine differences in brain dimensions in healthy elderly men and women during life, a CT method was developed to determine volumes of individual brain structures in healthy volunteers. Significant differences were noted in brain size and in the volumes of the lateral cerebral ventricles. These results show distinct sex differences in brain mass and are used to evaluate brain atrophy in **Alzheimer's** disease.

16. Sensation and Perception

vision -- Studies of risk factors for the development of glaucoma, cataracts, and macular degeneration with age are underway in the BLSA. Opacities of the cortical, nuclear and posterior lens were not associated with a history of myocardial infarction, angina or EKG evidence of coronary artery disease in 622 women and men. With respect to a broad range of nutritional variables, a higher level of calcium intake as measured by dietary diary was associated with a lower risk for nuclear opacities in both women and men.

Hearing -- Longitudinal studies indicate that hearing declines less rapidly in women than in men. These differences in rates of decline indicate that at the higher speech range frequencies (approximately 2,000 hertz), the rates of decline in hearing

sensitivity were about two times greater in men than in women. It appears that women are more resistent to age-related hearing loss.

Oral Sensory Function -- Studies on threshold and suprathreshold taste function for the four basic taste qualities (sweet, salty, sour, bitter) show that there is no general pattern of functional changes observed with increased age in women. Olfactory performance data indicates a generalized decreased function in older aged men and women. Participants across the life span are equally able to identify texture and temperature differences; however, aging brings a specific decline in the perception of localized lingual pressure.

17. Cell Replication

Understanding the mechanisms by which aging is regulated requires careful dissection of changes that may occur at the cellular level. A central research question is the relationship between senescence of cells in culture and aging of the individual: in particular, how changes in the ability of human cells to replicate in culture may be related to the age of the cell donor. A study of the replicative capacity of 600 fibroblast cultures derived from skin biopsies of BLSA women and men over a ten year period was recently completed, and the results are being readied for publication. The primary finding suggests that the major decrease in the replicative potential of cells from both BLSA women and men occurs after the third decade of donor age. The design of methods and studies to augment cultures sampled longitudinally and to examine the mechanisms underlying cellular senescence are underway.

Subcultures from over 300 of these BLSA skin fibroblast cultures have been banked at the NIA Aging Cell Repository and made available to members of the extramural scientific community. The value of these BLSA cell cultures, as well as other biological samples derived from BLSA participants and banked for subsequent analyses, will only increase as changes in health status, diseases acquired, and ultimately the cause of death become known through longitudinal follow-up.

18. Personality, Stress and Coping, and Women's Health and Well-Being

Personality traits -- individual differences in enduring emotional, motivational, and interpersonal styles -- are of central importance to an understanding of adaptation to stress, psychological well-being, and health behaviors. BLSA research themes concern the quantification of the basic dimensions of personality, their stability with age, as well as the coping processes by which individuals deal with stress. BLSA scientists have determined that in virtually all cases; women show the same wide range of individuality that men do, with a variety of strengths and weaknesses, needs and abilities. In general, BLSA research indicates that the

same structure of personality is found in adult women as in men: that women generally cope with stressful losses, threats, and challenges in the same ways; and that in women, as in men, health complaints are influenced by personality and psychological states.

In one BLSA study, 193 women, initially aged 23 to 86, were administered the Guilford-Zimmerman Temperament Survey, a measure of 10 personality traits. When readministered the same instrument 4 to 10 years later, they showed no change in average level. Thus, stereotypes that portray aging women as becoming increasingly depressed, withdrawn, rigid, cranky, or apathetic are without empirical foundation. Further, individuals maintain their distinctive characteristics as they age: the young extravert becomes the old extravert, and the conservative older women was probably just as conservative in her youth.

Studies on BLSA women have shown that the choice of coping mechanisms is a function both of enduring personality traits and of the requirements and opportunities of the particular situation. Both BLSA cross-sectional and longitudinal studies have shown that the ability to cope does not decline with age. Most older women are able to deal with the stress of bereavement and the consequent changes in their personal situation.

Personality traits have been shown repeatedly to be related to medical complaints, but it is often unclear whether traits contribute to the development of disease or simply to the readiness to perceive and report physical problems. In order to study these questions, personality must be measured in groups of individuals with objectively verified diseases. BLSA research has shown that in women, as in men, higher emotional distress is associated with more somatic complaints, a factor that should be considered in evaluating the validity of self-reports of health, and may contribute to symptom presentation in such disorders as irritable bowel syndrome. Of particular interest for future research are the questions of whether antagonistic hostility is associated with coronary disease in women as it is in men, and whether personality traits can predict the occurrence or course of Alzheimer's disease.

BLSA studies have shown that normal personality traits are powerful predictors of both psychological well-being and psychopathology. Indeed, **personality traits** are better predictors of well-being than are age and sex combined. These results are useful to counselors, clinical psychologists, and psychiatrists who can use information on personality traits to understand their patients, select appropriate therapies, and anticipate the course of therapy.

IV. OPPORTUNITIES, INITIATIVES, AND RECOMMENDATIONS IN WOMEN'S HEALTH RESEARCH

There are inevitably more research opportunities available than can be actively pursued. Research on health issues relevant to older women is no exception. The following pages outline selected research areas of particular relevance to women that (1) are currently being supported but that could benefit from expansion, or (2) need but do not have a significant knowledge base from which decisions affecting women's health may be drawn.

1. Studies of Menopause

The NIA supports studies on the menopause and hormonal changes with age. There are nonetheless many questions and potential topics for further research that are not currently being investigated to any significant degree. A major focus for future research would be the mechanisms of changing hormone effects at the molecular biological level and the health implications of such effects on older women. For example, what happens at the molecular biological level in bone cells when estrogens disappear in menopause? Similarly, what happens to the cellular production of bone growth factors? Would the changes seen at the cellular level be the same or different in women who participate in active exercise regimens compared with those who do not? Moreover, especially little is known about how the social and behavioral world of women affects and is affected by hormonal changes with age.

In a collaborative project involving the NIA intramural research program, 1,25-dihydroxycholecalciferol (an active vitamin D metabolite) administered to ovariectomized and non-ovariectomized post-breeding female rats produced bone loss in the ovariectomized animals and bone aain in the non-ovariectomized animals. This illustrates the general point that the pharmacodynamic and clinical response to various drugs and other hormones may be modified by the presence or absence of estrogens in humans. There is a significant lack of studies addressing the specific pharmacology involved in such responses in older women; this is clearly an important research area to pursue.

NIA grant-supported research on the menopause includes the Massachusetts Women's Health Study, the largest prospective investigation of a representative sample of middle-aged women presently available. This study is following some 2500 women transmenopausally and is providing new information that will add to our limited knowledge about this aspect of women's health. Findings from other studies in the biomedical area suggest that

estrogens may have a beneficial effect on neuronal function; conversely, the cessation of estrogen function at menopause may be followed by a decrease in neuronal function. This is an important area for further study, especially at the cellular level.

INITIATIVES/RECOMMENDATIONS: Future directions call for continuing longitudinal studies of women going through menopause, and of how behavioral and social factors interact with biological processes to affect the health and functioning of women and their families. Current NIA research interests include the possibility of establishing a special population of peri-menopausal women as a complementary study to the BLSA so that the effects of the menopause, and possible interventions, can be studied longitudinally with a multidisciplinary approach. Changes in the bone, cardiovascular system, metabolism, hormones, immune function, collagen, strength, fitness, body composition, and psychological and sociological variables could be investigated to differentiate the effects of menopause from those of aging, and to compare changes seen in these women to those seen in men of comparable ages. The interrelationships between these variables and the way these interactions change with aging and the menopause would give added insight into how women age. This initiative will be pursued as resources permit.

2. Osteoporosis

The enormous public health impact of osteoporosis continues to grow. This burden is concentrated heavily among women over 70 years old. In particular, the vast majority of hip fractures occur in this group, causing hospitalization and temporary disability for approximately 200,000 persons per year, and long-term loss of independence for a significant proportion of these. Evidence is increasing that the osteoporosis disease process may differ in significant respects in persons aged 70 or more compared to younger ages, yet much remains to be learned about mechanisms accounting for these differences. The NIA supports an expanding program of osteoporosis-related research focusing on cause and progression of the disease together with treatment and prevention.

INITIATIVES/RECOMMENDATIONS: Current NIA research on osteoporosis is primarily individual investigator-initiated research. A valuable additional step would be clinical trials of combinations of possible interventions and treatments (such as calcium supplementation, estrogens, and other agents such as etidronate; and exercise) which could alleviate or perhaps eventually prevent the most serious manifestations of the disease. The NIA has recently solicited applications for cooperative agreements to develop and test interventions to lessen, prevent, or reverse loss of bone strength in the hip to reduce risk of hip fractures in older persons. Related companion studies will focus on mechanisms underlying the interaction of the disease processes in older people with interventions being explored in the cooperative agreements.

The **NIA** also proposes to study hormonal stimulation of **bone** formation in older men and women. Testing would focus on the effects of growth hormone alone, growth hormone plus estrogen, insulin-like growth -factor, and such regimens as growth hormone releasing hormone or dietary arginine/lysine. In particular, the dietary supplements would be tested for their ability to stimulate the release of growth hormone and whether one is able **to** restore the normal periodic secretion of this factor.

3. Frailty and Disability

Physical frailty is responsible for a large share of the need for long-term care by older individuals. As they age, many older women and men become unable to perform many of the normal physical activities of daily living. This may be due to frailty and its accompanying disability, disease, psychosocial factors, or a combination thereof. A better understanding of this mix is fundamental to developing strategies for alleviating or modifying disability.

INITIATIVES/RECOMMENDATIONS: BLSA research findings have suggested a number of possible areas for research on interventions designed to delay, retard, or even reverse the progression of processes that result in increasing frailty and disability. Among the most promising is a study of the role of physical activity in favorably influencing a wide variety of functions. Sufficient preliminary data have been assembled to warrant a more intensive effort to define the types, intensities, durations, and frequencies of activity needed to have significant effects on muscle strength, endurance, bone density, serum lipids, glucose tolerance, cardiovascular and pulmonary function, atherogenesis, and psychological health and well-being.

In FY 1990, the NIA and the National Center for Nursing Research initiated a major, long-term program of clinical trials on intervention techniques to reduce frailty and its associated injuries. These studies will focus on reducing long-term care needs and injury risks associated with physical frailty. More recently, the NIA published a Request for Applications (RFA) for research projects on physical frailty in minority older populations.

In FY 1991, the NIA will fund a Women's Aging Study to identify and follow 1,000 disabled older women over a three-year period. The overall goal of this study is to identify a population of non-institutionalized **women age** 65 and older who have moderate to severe physical disability. These women will be comprehensively evaluated to gain an understanding of the diseases and conditions **responsible for** their disabilities, and **will then be followed** prospectively over a three-year period. A **subset of the survey**

population will receive intensive followup, with weekly contacts to assess short-term changes in functional status.

4. **Studies** of Dementia and Women

AD is an age-associated disease. The prevalence of **Alzheimer's** disease increases with age in virtually all population based investigations. Several well conducted studies have reported that the prevalence (number of cases at a given point in time) of Alzheimer's disease is, in fact, hiaher in women than in men. The question remains: Are-age-specific-incidence rates (number of **new** cases in a given time period) in fact higher for women than men? If this clinical observation is confirmed in population-based studies, it may lead to new hypotheses about the etiology of the disease. The oldest old, primarily a female population, shows a striking increase in the incidence of Alzheimer's disease, with the possibility that this disease is becoming nearly universal with advanced age.

INITIATIVES/RECOMMENDATIONS: The NIA plans to encourage research which will address the question of whether women are at a greater risk for Alzheimer's disease than men. In particular, the NIA plans to study a large number of women and men over age 85, including assessment of their mental status. Careful attempts will be made to distinguish dementia caused by Alzheimer's disease from that resulting depression or other disorders.

It has been suggested that estrogen treatment may act as a prophylaxis for dementia, because women undergoing estrogen **treatment** were found to have a lower than expected rate of dementia. A **three-**year human autopsy study has just been funded that will examine the **neuronal** hypertrophy in the infundibular nucleus, associated with menopause and ovariectomy. It appears that this hypertrophy is an adaptive response to the ovarian failure and loss of circulating estrogens.

5. Studies of Cancer in Older Women

People aged 65 and older have disproportionately high **rates of** cancer incidence and mortality. The NIA and the National Cancer Institute (NCI) have had several discussions concerning increased coordination of research on cancer in older people. Recent **NIA-NCI** activities have included a workshop on the underlying molecular, cellular and immunological factors in age-related cancers (June 1990); and release of a program announcement to stimulate investigator-initiated research in these areas. A Forum on Breast Cancer Screening in Older Women was held June 1990, and is producing discussions regarding co-funding of a request for applications on behavioral issues in breast cancer screening. In addition, the NIA is considering the possibility of several workshops on cancer in older people in FY 1991, including a workshop on breast and

gynecological cancers in older women, and a workshop focusing on older-aged cancer survivors which would emphasize women's health status.

Since 1978, the BLSA has collected blood samples from women participants on each visit. Frozen and lyophilized plasma and serum samples have been banked for subsequent analysis as new assays are discovered or new research opportunities arise. The longitudinal follow-up of BLSA women allows identification of a subset of women who, since their initial entry into the study, have been diagnosed with cancer. An opportunity exists to withdraw serum samples obtained from these women over sequential visits from the BLSA bank, and undertake a search for blood markers of certain cancers -- including breast, endometrial, and ovarian. The identification of such blood markers, if successful, could aid in early diagnosis.

INITIATIVES/RECOMMENDATIONS: The NIA Epidemiologic Studies of the Elderly (EPESE) program is a multi-center prospective study of community-dwelling older people. In FY 1991, the Surveillance, Epidemiology, and End Results (SEER) Program, a population-based national tumor registry, will be used to verify the cancer diagnosis reported by the EPESE cohort in two rural counties in East Central Iowa. A data base will be created on EPESE participants who have indicated that they have been hospitalized overnight with cancer on baseline and in subsequent telephone and follow-up interviews. (Those hospitalized included 259 women.) These data will be linked with data on the characteristics of their cancer and its treatment from the Iowa SEER tumor registry. The merging of these two data sets will provide the potential for powerful descriptive and analytical epidemiologic studies to expand the knowledge base on cancer in the elderly in a population-based noninstitutionalized sample of persons in a rural setting.

A second EPESE site at Duke University has also reported the prevalence of cancer and the proportion of those reporting cancer who indicated that they were hospitalized overnight or longer for this condition. Rates of cancer among black persons were about half those of white persons, and rates for black women were slightly higher than those for black men. In the upcoming in-person interview, investigators propose to ask a series of questions concerning screening for breast cancer and to focus additional inquiry on the population's response to signs and symptoms of disease. The latter effort is expected to capture incident cancers and recreate the trajectory that brought individuals into the health care system.

As part of the NIA's expanding initiative in cancer and aging, a workshop on Perspectives on Ovarian Cancer in Older Women is planned for September 1991. The goals of the workshop are to increase our knowledge of the etiology, (particularly with regard

to age-related risk factors), diagnosis and treatment of cancer in older women.

6. Epidemiologic Studies

NIA-supported longitudinal epidemiologic studies are a major source of information about the older population. The NIA has and continues to support a number of large scale longitudinal studies concerned with health and functioning of older adults that include representative samples of older women.

The four on-going Established Populations for Epidemiologic Studies of the Elderly (EPESE) evaluate prevalence and severity of, and risk factors for disability -- as well as social, behavioral, and environmental conditions related to the health problems of older women and men -- and how they differ by age, sex, race, and socioeconomic status. The National Health and Nutrition Examination Survey Epidemiologic Followup Study (NHEFS), supported in large part by NIA, was initiated in 1982. Its goal was to examine relationships between physiological, nutritional, and demographic factors and morbidity and mortality. The NHEFS will continue in 1991 to collect data on various health outcomes, functional limitations, institutionalization, and mortality. With a national probability sample of several thousand elderly women, this data affords significant opportunity to study a broad range of factors relevant to women's health.

While these studies do not represent new initiatives, followup studies continue and the wealth of analytic opportunities they afford exceeds current capacity to fully utilize them. Although a number of reports have been published using these data, much current and future work focuses on additional analytic investigations of relationships among physiological, social and environmental factors and health outcomes.

INITIATIVES/RECOMMENDATIONS: As previously described, the NIA will fund the Women's Aging Study in FY 1991. This study will comprehensively evaluate a sample of 1,000 women to gain an understanding of the diseases and conditions responsible for their disabilities. Ideally, depending on the availability of resources, a second examination site will be established in the future. A second site would provide an increased sample size and allow greater refinement of research hypotheses, possible cultural and racial comparisons and, potentially, indicate important health status trends.

7. Preventive Health Behaviors

Women, on average, engage in more preventive health behaviors than men. They are also quicker to respond to illness symptoms. These behaviors are often cited as one of the reasons women live longer

than men. Yet, older women are not engaging to the same degree as younger women in some preventive health behaviors that are strongly linked to positive health outcomes. For example, older women are more likely to get breast cancer than younger women, but are much less likely to engage in breast self exam or get regular mammograms.

INITIATIVES/RECOMMENDATIONS: A concerted research effort is needed to understand why older women have lower rates of preventive health behaviors than younger women for breast cancer and other conditions to which they are particularly vulnerable. What, for example, is the role of socioeconomic factors, health perceptions, social supports, attitudes about aging, or current medical practices? What behavioral or social interventions are effective in motivating older women to make greater use of preventive health services? How can health care professionals' use of such preventive strategies with older women be increased?

8. Women as Caregivers

Women continue to be the primary and most likely caregivers for dependent older people. Our research has shown that the pivotal factor in an older person's care and continued community living is the presence of an adult daughter. Nevertheless, with demographic changes such as changes in fertility, employment, marital stability, and geographic mobility, women's availability to serve as caregivers may also be changing. To date, little research has focused on interventions specifically directed to such women. Building on research showing that caregivers often find their responsibilities rewarding and that family care is preferred by older people, studies of innovative workplace, community, or family services might identify ways to prevent or alleviate the strain that may affect women caregivers as they perform these multiple roles.

INITIATIVES/RECOMMENDATIONS: On-going research on informal care for older people requires research on women as the primary caregivers for dependent older people. However, dramatic changes in family size, increased longevity of dependent older people, coupled with the greater workforce participation of women, indicate the need for continuing studies of gender differences in caregiving. Research is needed that investigates how care responsibilities may be shared by family members; under what conditions men, rather than women, are likely to be caregivers; how employed women balance care and other responsibilities; and how the special burdens of Alzheimer's Disease affect older women caregivers.

One component of the NIA Honolulu Aging and Dementia Study scheduled for 1991, consists of an interview of spousal caregivers of demented men. The interview will include, among other topics, questions with regard to burden of caregiving. Studies of caregiv-

ing are important also in development of interventions to assist family caregivers and maintain frail elders in their homes.

9. Work and Retirement

Patterns of work and retirement among older women differ markedly from those of older men, and appear to be increasingly distinct. For example, although national data show a continuing, longterm decline in the proportions of older men within the total workforce population, there is no parallel decline in paid employment among older women. Additionally, women's retirement patterns are only now emerging because proportions of women in the labor force, which were low early in the century, have been rising rapidly for several decades and will predictably continue to rise. Work and retirement patterns may also be affected because women have consistently been paid at lower rates than men, even for comparable jobs. For the future, data indicate that cohorts of women workers who will be old in later decades are likely to have higher retirement income because of improvements in pay to women workers.

Retirement patterns among older women have strong implications for future health policy decisions, including policies affecting Medicare, Medicaid, and other federal programs directed toward the older population. Consequently, the dramatic differences between women and men in patterns of work and retirement and continuing rapid changes in women's participation in the workforce suggest the need for increased and targeted research in this area.

INITIATIVES/RECOMMENDATIONS: Research on women's roles examines changing patterns of later-life work and retirement as they affect health, productivity, and independence. Research in this area has concentrated mostly on the immediate impact of retirement on men. However, patterns of work and retirement among older women differ markedly from those of men, and appear to be increasingly distinct. Also, the rising proportion of dual earner households means that future research must examine work and retirement as a household process.

The NIA, in collaboration with the University of Michigan, has begun to design a long-term study of health and retirement issues affecting both men and women. Families in the survey will be asked about work history, earnings, assets and debts; pension rights and retirement incentives offered by employers; health conditions and disability status: family structure; housing conditions: and current and prospective living standards. Data collected through this study will provide policy-makers and the research community with badly needed current and continuing information about the causes and consequences of retirement.

10. Older Minority Women

Compared with either minority men or non-minority men and women, older minority women are more likely to be impoverished, suffer greater disabilities, and to live alone than other older individuals. However, there is little detailed information on the circumstances affecting such disadvantage among minority women, or their needs for health and other services. Even their contributions to their families and communities through child and elder care are poorly documented or understood. Neglected also is how patterns of family structure, immigration and migration, age and sex ratio, and expectation for employment affect specific populations of older minority women. Thus, both the needs and contributions of minority women as they age requires increased research effort.

INITIATIVES/RECOMMENDATIONS: Research is needed on intergenerational relationships and the contributions of minority women to their families and donununities through caregiving for dependent children and other relatives. An initiative on long term care and minority aging is under consideration to encourage targeted studies of informal care networks among older minority women, patterns of formal care services, and possible barriers to appropriate formal long term care.

11. Older Women in Rural Environments

Recent research suggests that older rural residents have unique needs and are a neglected area of investigation. In rural areas, older people in general are more likely than their urban counterparts to be in poor health, to suffer from chronic or serious illness, and to be without a regular source of health care and health insurance. Within this population, older rural women by far outnumber men, and on average may represent a category whose greater disability, increased likelihood of living alone, and poorer access to health and community services require special targeted efforts.

Further research is needed to provide information about the changing characteristics of the older rural population of women, including, for example, the population structure of aging women in rural communities; the availability, utilization, and quality of health-care and other services for women: differences in the needs and capabilities of particular groups of women: and aging rural women as resources for themselves and others.

INITIATIVES/RECOMMENDATIONS: The NIA currently supports two centers of specialized studies on rural aging. Within these centers, and in plans for a third rural aging center, special attention will be given to research that focuses on the changing characteristics of the older rural population of women. These

studies will include, for example: the population structure of aging women in rural communities; the availability, utilization, and quality of health care and other services for women: differences in the needs and capabilities of particular groups of women; and aging **rural women as resources for themselves and others. Such studies are a necessary part of planning for services and programs for older rural residents.**

V. CONCLUSION

The National Institute on Aging supports a broad array of research both directly and indirectly related to the health needs of older women. As this report demonstrates, the BLSA is contributing new insights into how and why women age, and is documenting both similarities and subtle or profound differences between men and women. For example, age-related adaptations in cardiac structure and function have been shown in both women and men; the deterioration of glucose tolerance which occurs in old age, independent of increasing fatness and decreasing fitness, is similar in BLSA women and men; and both women and men maintain their distinctive personality characteristics as they age. Conversely, illustrative of the sex differences which have been revealed to date are differences in body fat distribution patterns which may account, in part, for women's more favorable morbidity and mortality experience; evidencethatwomen's smaller muscle mass may be the major factor in their lower maximal aerobic capacity; and women's greater resistance to age-related hearing loss.

These results reinforce a central BLSA finding: age does not mean a universal and inevitable decline in all physiologic and psychological functions. Rather, different organs, different systems, and different individuals age at different rates. This great diversity has clinical implications and offers the opportunity to devise interventions to increase the health, functioning, and well-being of older women. For example, precipitous changes in variables such as salivary gland function and personality (which BLSA research has shown remain essentially stable over the lifespan) are likely to be manifestations of a pathological condition.

The role of the BLSA in contributing new knowledge directly relevant to improvements in women's health and well-being is exemplified by the following examples.

- Diaanosis of disease. In otherwise asymptomatic BLSA women the presence of exercise-induced myocardial abnormalities, accompanied by an abnormal thallium scan, identifies a group of individuals with a strikingly high incidence of subsequent coronary events.

- Preventive health care. The finding that virtually no BLSA women over age 55 have antibody to Tetanus Toxoid suggests that current immunization practices should be rethought for older women.

- Individual health behaviors. BLSA women who smoke preferentially deposit fat in the abdominal area (an adverse fat distribution pattern for health outcomes). This adds yet another factor in favor of discontinuing smoking.

- Women's psychological well-being and role in society. BLSA research indicates that most older women are able to deal with the stress of bereavement and that stereotypes which portray aging women as becoming increasingly depressed, withdrawn, rigid, cranky, or apathetic are without foundation.

As is the case in most fields of scientific endeavor, current NIA research on older women's health issues reflects only a portion of the total range of research opportunities. The NIA strongly supports the interest in and need for further research on older women's health issues. Over the next several years, the NIA plans to expand research efforts in on-going activities, including the BLSA, and implement a variety of new projects as resources permit. In addition, to the extent possible, selected research areas outlined in the initiatives section of this report will be targeted for further effort.

APPENDIX

ANNOTATED BIBLIOGRAPHY

This bibliography contains publications by scientists affiliated with the Baltimore Longitudinal Study of Aging (BLSA). In most cases, the research reported is based in whole or in part on studies involving BLSA women. In addition, publications reporting on selected research directly relevant to women's health and conducted with non-BLSA women are included and identified as such.

Postmenopausal Hormone Replacement Therapy

(Clinical Research by BLSA Investigators Conducted in Special Populations)

Harman SM, Blackman M. The female. In: **JG** Evans, TF Williams, eds., The Oxford Textbook of Geriatric Medicine. London: Oxford Medical Publications, (In Press).

Bellantoni MF, **Harman** SM, Cho DE, Blackman MR. Effects of progestin-opposed transdermal estrogen administration on GH and IGF-I in postmenopausal women of different ages. **J** Clin Endocrinol **Metab,** (Jan 1991, In Press).
Estrogen replacement by skin patch **(Estraderm®)** plus oral **Provera®** produced similar increases in young vs. older women in blood estrogen levels, no effects on circulating basal growth hormone (GH) and insulin like growth factor-I (IGF-I) levels, and a decrease in release of growth hormone after stimulation with growth hormone releasing hormone.

Bellantoni MF, **Harman** SM, Cho D, Blackman MR. Transdermal estrogen replacement therapy does not alter basal somatomedin-C or GH levels, or GH responsivity to GHRH, in postmenopausal women of different ages. The Endocrine Society, Seattle WA, June 21, 1989, (Abstract **#783).**
GKRH-stimulated growth hormone levels in postmenopausal women are inversely correlated with both age and body mass index, but are not altered by transdermal estrogen replacement therapy.

Bellantoni MF, Engelhardt SM, **Harman** SM, Blackman MR. Benefits and adverse effects of hormone **replacement therapy** in younger and older postmenopausal women. American Geriatric Society Meeting, Atlanta, GA, April 1990, (Abstract # P-24).
Older postmenopausal women experienced beneficial effects of hormone-replacement therapy with relatively mild adverse effects.

Bellantoni MF, **Harman** SM, Neer RM, Blackman MR. Transdermal estrogen replacement therapy exerts similar effects on calciotropic

hormone economy in younger and older postmenopausal women. The Endocrine Society, Atlanta GA, June 20 -22, 1990, (Abstract # 505). Estrogen replacement by **skin patch (Estraderm®) plus oral Provera® exert similar** effects on serum and **urine calcium and serum parathyroid hormone** (PTH) **in healthy younger and older postmenopausal women which are mediated primarily by the effects of estradiol and result mainly from a decrease in bone calcium resorption, 'with .a compensatory rise in serum PTH.**

Bellantoni MD, **Harman** SM, Blackman MR. Age-related decreases in basal and estrogen-modulated levels of **LH,** but not FSH, in healthy postmenopausal women. The Gerontological Society of America, 43rd Annual Scientific Meeting, November **16-20,** 1990, (Abstract **#167).** In healthy postmenopausal women, basal plasma levels of **luteinizing hormone, but not follicle stimulating hormone,** decrease **with age,** and **this differential is maintained during suppression with transdermal estradiol replacement therapy.**

Behavioral Treatments for Incontinence **in Women**

(Publications reporting results involving non-BLSA research participants unless otherwise indicated)

Burgio KL, **Engel** BT, **Locher** JL. Normative patterns of diurnal urination across six age decades. J Urology, (In Press). Analysis of the patterns and frequency of diurnal urination in BLSA women and men shows that the clinical definition of urinary frequency must be age-adjusted.

NIA intramural scientists have developed powerful, behavioral treatments for the most common kinds of incontinence occurring in community-dwelling elderly. In studies of 90 patients, 77 of whom were women, approximately an 80% improvement in bladder function using behavioral training methods was found. These results are described in the following publications:

Whitehead WE, Burgio KL, **Engel** BT. Biofeedback treatment of fecal incontinence in geriatric patients. J Am Geriatr **Soc** 1985, 33: **320-324.**
Biofeedback of anal sphincter activity is **the** treatment of choice for many causes of fecal incontinence: age is not a limiting **factor for therapy.**

Burgio KL, Whitehead WE, **Engel** BT. Behavioral treatment of **urinary incontinence** in the elderly: bladder-sphincter biofeedback and toileting skills training. Annals of Inter Med 1985, 104: 507-515.
Behavioral treatment of urinary incontinence in community-dwelling elderly patients.

Burgio KL, Robinson JC, **Engel** BT. The role of biofeedback in Kegel exercise training for stress urinary incontinence. Am J

Obstetr and Gynecol 1986, **154:58-64.**
Behavioral treatment of stress incontinence.

Burton JR, Pearce KL, Burgio EL, **Engel** BT, Whitehead E. Behavioral training for urinary incontinence in elderly ambulatory patients. J Gerontol Nurs 1988, **14:31-34.**
Behavioral treatment of urinary incontinence in elderly, ambulatory patients by a nurse in an office practice.

Burgio KL, **Engel** BT. Biofeedback-assisted behavioral training for elderly men and women. **J** Am Geriatr **Soc** 1990, **38:338-340.**
Review of behavioral treatments of incontinence in **community-**dwelling adults.

Approximately 50% of nursing home residents are incontinent. A combination of behavioral treatments and staff management procedures has been developed and evaluated to improve and maintain improvements. in continence in elderly nursing home residents. Relevant publications include:

Burgio LD, Burgio KL, **Engel** BT, **Tice** LM. Increasing distance and independence of ambulation in elderly nursing home residents. J Appl Behav Analysis 1986, **19:357-366.**
Some wheelchair restricted residents can be trained to increase their ambulation and independence.

Butler F, Burgio LD, **Engel** BT. A behavioral analysis of geriatric nursing home patients receiving neuroleptic medication: a comparative study. **J** Gerontol Nurs 1987, 13: 15-19.
Elderly nursing home residents whose behaviors are noxious to the staff are more likely to receive neuroleptic medications; despite these medications they continue to manifest adverse behaviors, and they also have significant, medication-related side effects.

Burgio LD, Jones LT, Butler F, **Engel** BT. Behavior problems in an urban nursing home. J Gerontol Nurs 1988, **14:31-34.**
An analysis of behavioral problems of elderly nursing home residents.

Burgio LD, Jones LT, **Engel** BT. Studying incontinence in an urban nursing home. **J** Gerontol Nurs 1988, **14:40-45.**
Correlates of incontinence in nursing home residents.

Burgio LD, Butler F, **Engel** BT. Nurses' attitudes towards geriatric behavior problems in long-term care settings. Clin Gerontologist 1988, **7:23-34.**
An examination of the attitudes of 101 geriatric nurses toward behavior problems of residents in 5 long-term care facilities.

Burgio LD, **Engel** BT, McCormick **KA,** Hawkins A, **Scheve** A. Behavioral treatment for urinary incontinence in elderly inpatients: initial attempts to modify prompting and toileting

procedures. Behav Therapy 1988, **19:345-347.**
An **examination of** the efficacy of a behavioral intervention for treating incontinence in a long-term care setting.

Burgio LD, **Engel** BT, Hawkins A, McCormick **KA,** Scheve A. A descriptive analysis of nursing staff behaviors in a teaching nursing home: differences among nursing aides, licensed practical nurses, and registered nurses. The Gerontologist 1990, 30:107-112.
Provides an analysis of nursing staff behaviors in a teaching nursing home based on a sampling of various staff behaviors 7 times a day, 5 days a week over 37 months.

Engel BT, Burgio LD, McCormick **KA,** Hawkins AM, Scheve **AAS,** Leahy E. Behavioral treatment of incontinence in the long-term care setting. **J** Am Geriatr **Soc** 1990, **38:361-363.**
Analysis of staff management procedures to treat incontinence in the nursing home.

McCormick **KA, Cella** M, Scheve A, **Engel BT.** The cost effectiveness of treating incontinence in severely mobility-impaired long-term care residents. Quality Review Bulletin 1990, **16:439-443.**
The treatment of incontinence in severely mobility-impaired nursing home residents can result in significant cost savings.

Burgio LD, **Engel** BT, Hawkins A, McCormick **KA,** Scheve A, Jones LT. A staff management system for maintaining improvements in continence with elderly nursing home residents. J Appl Behav Anal **1990,23:111-118.**
A staff management system for maintaining treatment gains achieved on a specialized continence unit located in a geriatric nursing home was effective in maintaining prompted voiding activities with corresponding maintenance **of** improved patient continence.

Petrucci K, McCormick XA, Scheve A. Documenting patient care needs: Do nurses do it? **J** Gerontol Nurs 1987, **13(11):34-38.**
and
Palmer RN, McCormick **KA, Langford** A. Do nurses consistently document incontinence? **J** Gerontol Nurs 1989, **15:11-16.**
Incontinence is not consistently documented in nursing home residents' medical records: care plans are not consistently developed for managing incontinence.

<u>Women's Cocrnitive **Aging** and **Alzheimer's** Disease</u>

A **BLSA** study of 108 women and 176 men ranging in age from 18 to 91 years of age examined sex-differences in sustained attention. Although women were slower in their responses to the appearance of targets than men, women were equally accurate in detecting rarely occurring targets over a 60 minute period. However, there were no sex differences in rates of forgetting. These findings have been reported as follows:

Giambra LM, Quilter RE. Sex differences in sustained attention across the adult life span. J Appl Psycho1 1989, 74:91-95.

Giambra LM, Arenberg D. Age differences in sentence memory and forgetting. Presented at the annual meeting of the Psychonomic Society, 1990.

Complaints about "declining memory with advancing age are so common that they may appear normal to both layman and professionals. Although there is evidence to suggest that many facets of cognitive performance decline over the adult lifespan, the prevalence of memory complaints is probably far lower than our stereotypes of memory loss and old age might lead us to believe. Studies of BLSA participants have found that memory complaints are unrelated to actual memory performance: they are associated with characteristic tendencies toward somatic complaining and psychological distress in both men and women. Women were no more likely to complain about declines in their memory than were men: Zonderman AB, Costa PT Jr, Kawas CH. Personality predicts complaints of benign memory loss. Presented to the American Academy of Neurology, Chicago 1989.

Studies of the early markers of Alzheimer's disease in BLSA participants have identified simple recall tasks as potential predictors of subsequent cognitive impairment. In these studies, impairments in recognition memory and immediate free-recall performance were equally good predictors of cognitive impairment in women as in men, and there were no differences in the rates of cognitive impairment between men and women. These BLSA results have been presented to and reported in:

Costa PT Jr, Kawas CH, Zonderman AB. Impairment in recognition memory performance as a correlate of cognitive status in the Baltimore Longitudinal Study of Aging. Presented to the National Academy of Neuropsychology 1990.

Kawas CH, Costa PT Jr, Zonderman AB. Immediate and delayed free recall performance as longitudinal predictors of cognitive status. Presented to the National Academy of Neuropsychology 1990.

Fozard JL, Mullin PA, Giambra LM, Metter EJ, Costa PT Jr. Normal and pathological age differences in memory. In: JC Brockelhurst; London: Churchill Livingstone, (In Press).

[The NIA intramural program has a major multifacted research effort underway on Alzheimer's disease and other dementias. Special populations of women and men are recruited and enrolled in these clinical studies; the extensive publications reporting research results have not been included in this bibliography but can be made available.]

Osteoporosis and Age Related Bone Loss

Plato C, Roy T, Sherman S, Tobin J. Bone mineral density in normal men and women: the effect of age at different bone sites. J Bone Mineral Res 1990, 5:697A, (Abstract).
While premenopausal women show no decreased bone with age at any of four bone sites studied, young men have a pronounced loss in the hip. In older postmenopausal women (60+ years), there is a faster loss of bone at each site studied when compared to men of the same age, although men also demonstrate significant loss.

Sherman S, Hollis B, Tobin J. Vitamin D status and related parameters in a healthy population: the effects of age, sex and season. J Clin Endocrinol Metab 1990, 71:405-413.
and
Sherman S, Plato C, Hollis B, Tobin J. Bone mineral density and related biochemical parameters in healthy men and women: age and sex contrasts. J Bone Mineral Res 1989, 4:1098A, (Abstract).
Age and sex differences in certain vitamins, minerals, and hormones thought to play a role in the modulation and control of bone metabolism were evaluated. The most dramatic sex difference was in serum phosphorous levels which were stable in women and declined in men.

Sherman S, Gundberg C, Hollis B, Plato C, Roy T, Tobin J. Low femoral density in young men: evidence for an age and gender specific high bone turnover state. J Bone Mineral Res 1990, 5:777A, (Abstract).
Biochemical parameters were related to age adjusted bone values in young and old BLSA men and women. Bone loss in older women was correlated to measures of high bone turnover.

Tobin J, Sherman S, Fleg J, Plato C. Peak Vo, is not an independent determinant of bone density in normal men and women. J Bone Mineral Res 1989, 4:1099A, (Abstract).
In both women and men across the age span, there was no relationship of age-adjusted performance on tests of VO_2Max (a measure of physical fitness) and bone mineral density.

Bellantoni MF, Blackman MR. Diagnostic screening for osteoporosis, a brief critique of techniques for detecting types I and II osteoporosis. Geriatrics 1988, 43:63-70.
A brief review of radiographic and biochemical methods for diagnosing osteoporosis.

BLSA Cardiovascular Research Involvinu Women

(Includes research findings on silent myocardial ischemia, cardiac structure and resting function, and physical fitness in women)

Fleg JL, Kennedy HL. Cardiac arrhythmias in a healthy elderly population: detection by 24-hour ambulatory electrocardiography.

Chest 1982, 81:(3), 302-307.
High prevalence of arrhythmia in healthy elderly; no sex differences except that 24 hours mean heart rate is faster in women.

Fleg JL, Gottlieb SH, Lakatta EG. Is digoxin really important in treatment of compensated heart failure? A placebo-controlled crossover study in patients with sinus rhythm. Am J Med 1982, 73: 244-250.
Digoxin could be successfully withdrawn from non-BLSA men and women outpatients with stable heart failure and normal heart rate rhythm despite mild deterioration in left ventricular performance off digoxin.

Rodeheffer RJ, Gerstenblith G, Becker LC, Fleg JL, Weisfeldt ML, Lakatta EG. Exercise cardiac output is maintained with advancing age in healthy human subjects. Circulation 1984, 69:203-213.
Assessment of hemodynamics in response to exercise.

Fleg JL, Lakatta EG. Prevalence and prognosis of exercise-induced nonsustained ventricular tachycardia in apparently healthy volunteers. Am J Cardiol 1984, 54:762-764.
Nonsustained exercise-induced ventricular tachycardia seen=4% of normals 65 years or older; No gender difference.

Fleg JL, Lakatta EG. Post-exercise hypotension: prevalence and significance of in apparently healthy subjects. Am J Cardiol 1986, 57:1380-1384.
Post-exercise hypotension - seen in 2.6% of men is 0.7% of women p=.07. Uncommon after age 55 (10 fold more common below age 55).

Tresch DD, Fleg JL. Unexplained sinus bradycardia: clinical significance and long-term prognosis in apparently healthy persons older than 40 years. Am J Cardiol 1986, 58:1009-1013.
Unexplained sinus bradycardia is seen in approximately 4% of apparently healthy BLSA participants over 40 years old. No gender difference, and this appears to be benign.

Bause GS, Fleg JL, Lakatta EG. Exercise-induced arrhythmias in diuretics-treated patients with uncomplicated systemic hypertension. Am J Cardiol 1987, 59:874-877.
Diuretic-treated hypertensive subjects have higher prevalence of simple exercise-induced premature ventricular beats (PVC's) than normotensive controls.

Renlund DG, Lakatta EG, Fleg JL, Becker LC, Clulow JF, Weisfeldt ML, Gersenblith G. Prolonged decrease in cardiac volumes after maximal upright bicycle exercise. J Appl Physiol 1987, 63: 1947-1955.
Cardiac volumes are lower after a bout of maximal cycle exercise than before exercise and this is prevented by beta adrenergic blockade.

Fleg JL, Lakatta EG. Role of muscle loss in the age-associated reduction in VO_{2max}. J Appl Physiol 1988, **65:1147-1151.**
Age-associated decline in VO_{2max} is nearly abolished if **VO_2 is normalized** for muscle mass rather than body weight in both sexes.. At any age, **VO_{2max} is** lower in women.

Busby MJ, Shefrin EA, Fleg JL. Prevalence and long-term significance of exercise-induced frequent or repetitive ventricular ectopic beats in apparently healthy volunteers. J Am **Coll** Cardiol 1989, **14:1659-1665.**
Frequent or repetitive exercise-induced **PVC's increase** exponentially with age in men but not in women, **but are benign in both sexes.**

Vaitkevicius P, Wright JG, Fleg JL. Effect of estrogen replacement therapy on the ST-segment response to postural and hyperventilation stimuli. J **Am Coll** Cardiol 1989, **64:1076-1077.**
Postmenopausal women on estrogen replacement show a greater prevalence of postural and post-hyperventilation ECG changes than age-matched women not on estrogen.

Josephson RA, Shefrin EA, Brant L, Lakatta EG, Fleg JL. Can serial exercise testing improve the prediction of coronary events in asymptomatic individuals? Circulation 1990, 81: 20-24.
A positive (ischemic) exercise ECG increases **the risk of a future** coronary event nearly **3-fold** in both sexes.

Fleg JL, Gerstenblith G, Zonderman AB, Becker LC, Weisfeldt ML, Costa PT Jr, Lakatta EG. Prevalence and prognostic significance of exercise-induced silent myocardial ischemia detected by thallium scintigraphy and electrocardiography in asymptomatic volunteers. Circulation 1990, **81:428-436.**
An ischemic exercise ECG and ischemic thallium scan in combination increase the likelihood of a future coronary event 3.6 fold, independent of conventional coronary risk factors in both sexes.

Fleg JL, **Das DN,** Wright J, Lakatta EG. Age-associated changes in the components of atrioventricular conduction in apparently healthy volunteers. J Gerontol: Med Sci 1990, **45:M95-M100.**
The ECG **P-R** interval (representing atrioventricular conduction time) prolongs modestly with age: this is due to delay proximal but not distal to the **His** bundle. At any age, the P-R interval is longer in men than women.

Lima JA, Fleg JL, Waclawiw M, Lima SD, Gerstenblith G. Cardiac structure and function in elderly women. Is there a distinctive profile? Circulation **1988, 78:(4)** Suppl. II, **II-63.**
Both older women and older men have thicker hearts than their younger counterparts, but there are no gender differences in wall thickness after normalization for body size.

Renlund DG, Gerstenblith G, Fleg JL, Becker LC, Lakatta EG. Interaction between left ventricular end-diastolic and end-systolic volumes in normal man. Am J Physiol 1990, 17: H473-H481.
End systolic left ventricular volume follows end diastolic volume closely in both sexes during postural shift, exercise or beta adrenergic blockade.

Danziger RS, Tobin JD, Becker LC, Lakatta EG, Fleg JL. The age-associated decline in glomerular filtration in healthy normotensive volunteers: lack of relationship to cardiovascular performance. J Am Geriatr Soc 1990, 38:1127-1132.
Creatinine clearance is not related to either systolic blood pressure, cardiac index or systemic vascular resistance in either sex.

Fleg JL, Rothfeld B, Gottlieb SH. Effect of maintenance digoxin therapy on aerobic performance and exercise left ventricular function in mild to moderate heart failure due to coronary artery disease: a randomized, placebo-controlled crossover trial. J Am Coll Cardiol, (In Press).
Discontinuation of maintenance digoxin did not cause a significant change in exercise capacity in stable outpatients with heart failure.

Fleg JL, Gerstenblith G, Becker LC, Coombs VJ, O'Connor F, Lakatta EG. Independent effects of age and gender on specificity of ejection fraction response to upright cycle exercise. Circulation 1990, 82:(Suppl. 3), 111-137.
Both increasing age and female sex independently diminish the increase in ejection fraction with exercise (LVEF) in healthy subjects, decreasing the specificity of LVEF for the diagnosis of coronary artery disease.

Fleg JL, Gerstenblith G, Becker LG, Clulow J, O'Connor F. Gender differences in exercise hemodynamics of older subjects: effects of conditioning status. Circulation 1990, 82: (Suppl. 3), 111-239.
Smaller resting and exercise ventricular volumes in older women are due to a lower fitness level. Women also have higher heart rates than men during vigorous exercise, but this is not attributable to a difference in physical conditioning.

Fleg JL, Kennedy HL. Prognostic significance of Holter monitoring, in apparently healthy older subjects. J Am Coll Cardiol, (Abstract, In Press).
In healthy older BLSA men and women, neither supraventricular nor ventricular arrhythmias on 24 hour ambulatory ECG predicted the development of future coronary events.

Immune Function and Susceptibility to Infectious Disease

Bender BS, Chrest FJ, Nagel JE, Adler WH. Peripheral blood CD8+

subsets in young and elderly adults: enumeration by two-color inununoflourescence and flow cytometry. Aging: Immunol and Infect Dis 1988, **1:23-29.**
There is a loss of the **CD8+** suppressor T **cell** population with **age,** but no difference between women and men.

Bender BS, Chrest FJ, Adler **WH.** Phenotypic expression of natural killer cell **associated** membrane antigens and cytolytic function of peripheral blood cells from different aged humans. **J** Clin Lab **Immunol** 1986, **21:31-36.**
There is no loss of natural killer (NK) cells -- cells which have the ability to kill tumor cells -- with age in either men or women. However, there are less **NK** cells and less **NK** cell function in young women as compared to young men.

Physical Fitness in Women

(Also see **BLSA** Cardiovascular Research on Women)

Fried LP, Fleg JL, Gundy E, **Tobin** JD, **Fozard** JL. Physical activity patterns of adults: changes by age and sex. Presented at the 42nd Annual Scientific Meeting of the Gerontological Society of America, Minneapolis, November 17-21, 1989, (Abstract).
Self-reported physiaal activity of 1,387 **BLSA** women and men indicate age and sex differences in patterns of physical activity and that physical activity ascertainment should include everyday activities in older adults.

Body Fat Distribution, Gender and **Longevity**

Shimokata H, **Tobin** JD, Muller DC, Elahi D, Coon PJ, Andres R. Studies in the distribution on body fat: I. effects of age, sex, and obesity. J Gerontol 1989, **44:M66-73.**
Five anthropometric ratios that classify individuals into different body types have been computed for 1179 BLSA men and women aged 17-96 years. In general, the age patterns show progressive trends toward increasing upper and central body fat deposition with age. In women, there tends to be a post-menopausal acceleration of this trend. The ratios are distinctly higher in men than in women and are also independently influenced by the body mass index.

Shimokata H, Andres R, Coon PJ, Elahi D, Muller DC, **Tobin** JD. Studies in the distribution of body fat. II. longitudinal effects of change in weight. Int **J** Obes 1989, **13:455-64.**
Men, as a group, have a more dangerous fat distribution pattern than women, but men as a group will show a more beneficial pattern of change in the waste hip circumference ratio with weight control than women.

Shimokata H, Muller DC, Andres R. Studies in the distribution of body fat: III. effects of cigarette smoking. **JAMA** 1989, 261:1169-

73; and Shimokata H, Muller DC, Andres R. Smoking wastes a good parisienne (Letter). JAMA 1989, 262:1185-6.
Effects of cigarette smoking in men are compared to studies in 289 BLSA women analyeed cross-sectionally. Women, who use weight control as their reason for continuing to smoke, are striking a bad bargain: their weights will be affected trivially, and they will add a worsening fat pattern to all of the other well-known haeards of cigarette smoking.

Shimokata H, Muller DC, Fleg J, Sorkin J, Ziemba AW, Andres R. Age as an independent determinant of glucose tolerance. Diabetes, (Jan 1991, In Press).
Fatness, fitness, and fat distribution can account for the decline in glucose tolerance from the young adult to the middle-aged years. However, age remains a significant determinant of the further decline in glucose tolerance of healthy old BLSA women and men.

Elahi D, Clark B, Andres R. Glucose tolerance, insulin sensitivity, and age. In: HJ Armbrecht, RM Coe, N Wongsurawat, eds., Endocrine Function and Aging. New York: Springer-Verlag 1990, 48-63.
Normative data derived from BLSA men and women are presented as a nomogram which allows simple derivation of age-specific percentile ranking for individuals across the adult age span of their two hour plasma glucose level after a glucose tolerance test.

Muller D, Tobin J, Andres R. A epidemiologic test of the hyperinsulinemia - hypertension hypothesis. Diabetes 1990, 39 (Suppl 1):147A, (Abstract).
The proposed link of hyperinsulinemia and hypertension was examined in 421 men and 228 women of the BLSA; the hyperinsulinemia hypothesis is not supported in this population.

Obesitv-Mortalitv in Populations Other Than BLSA: Data presented in the following three publications are derived largely from the Build Study 1979 of the insurance industry. In both men and women, there was a striking increase in "best weight-for-height" as age increased. An age-specific weight table was derived:

Andres, R. Mortality and obesity: the rationale for age-specific height-weight tables. In: WR Hazzard, R Andres, EL Bierman, JP Blass, eds., Principles of Geriatric Medicine and Gerontology, 2nd Ed. New York: McGraw-Hill, 1990, 759-65.

Andres R, Elahi D, Tobin JD, Muller DC, Brant L. Impact of age on weight goals. Ann Inter Med 1985, 103:1030-3.

Andres, R. Does the "best" body weight change with age?" In: AJ Stunkard, A Baum, eds., Perspectives in Behavioral Medicine, 1989, 7:99-107.

Nutrition

Hallfrisch J, Andres R, Muller D. Erythrocyte Superoxide Dismutase in the Baltimore Longitudinal Study of Aging. Fed Proc 1986, 45: 828, (Abstract).
Superoxide dismutase an enzyme which protects against oxidative damage declines in women with age.

Hallfrisch J, Muller D, Andres R, Singh VN. Plasma levels and supplement use of fat soluble antioxidant vitamins in the Baltimore Study. Gerontologist 1988, 28:230A, (Abstract).
The levels of Vitamin E and plant and animal sources of Vitamin A in blood increase with age in men and women. Plant sources of vitamin A are higher in blood of women than men, while animal sources of vitamin A are higher in men.

Hallfrisch J, Muller D, Singh V. Plasma and intake levels of ascorbic acid for men and women of the Baltimore Longitudinal Study of Aging. Gerontologist 1989, 29:187A, (Abstract).
Blood levels of vitamin C are higher in women than men and increase with age.

Hallfrisch J, Muller D, Drinkwater D, Andres R. Vitamin and mineral intakes from supplements and diet in men and women of the Baltimore Longitudinal Study of aging. FASEB J 1990, 4:A513, (Abstract).
Diets of women and men who take supplements are generally richer in vitamins and minerals without supplements than diets of those not taking supplements.

Hallfrisch J. Nutrition and aging in the Baltimore Longitudinal Study of Aging--selected mineral intakes. AGE 1990, (Abstract, In Press).
Substantial numbers of women do not obtain adequate amounts of calcium, magnesium, iron, and zinc from their diets.

Hallfrisch J. Nutrient intake recommendations for the older American-- selected vitamin intakes from the Baltimore Longitudinal Study of Aging. J Am Coll Nutr 1990, 9:540 (Abstract).
Diets of men and women provide more than adequate amounts of vitamins A, C, B_{12} and folacin, but may be low in E and B,.

Hallfrisch J, Muller D, Andres R. Macronutrient intakes and vitamin use in men and women of the Baltimore Longitudinal Study of Aging. The Gerontologist 1990, 30:326A (Abstract).
Diets of men and women who take supplements are higher in vitamins A, C, B,, folacin, magnesium and zinc before supplementation than diets of those not taking supplements.

Pulmonary Function

Beatty TH, Newill CA, Cohen BH, Tockman MS, Bryant SH, Spurgeon HA. Effects of pulmonary function on mortality. J Chron Dis 1985, 38(8):703-710.

Tockman MS. Effect of age on maximal forced expiratory effort and spirogram acceptability. Presented at the American Thoracic Society in Cincinnati OH, May 1989.
At least a component of the association of progressive FEV_1 impairment and subsequent cardiovascular mortality may be attributed to a decline in muscle strength.

Women's Oral Health

(BLSA and National Institute of Dental Research Collaboration)

Baum BJ. Characteristics of participants in the oral physiology component of the Baltimore Longitudinal Study of Aging. Community Dent Oral Epidemiol 1981, 9:128-143.
A description of demographic, socioeconomic and dental characteristics of 145 BLSA men and 109 BLSA women participating in the longitudinal study of oral physiology and aging. Dental data for women are presented by menopause status (pre-, post-).

Baum BJ. Current research on aging and oral health. Spec Care Dentist 1981, 1:105-109.
Comparatively little is known about oral physiology and aging, or about its corollary, the oral health problems of the elderly. Areas where research is needed are highlighted.

Baum BJ. Research on aging and oral health: an assessment of current status and future needs. Spec Care Dentist 1981, 1:156-165.
A review of the major generalizations of the aging oral cavity, discussing research findings, including BLSA discoveries, about oral mucosa, dental caries, oral motor behavior, salivary glands and saliva, and sensory function in both men and women.

Baum BJ. Evaluation of stimulated parotid saliva flow rate in different age groups. J Dent Res 1981, 60:1292-1296.
Among BLSA men and women, taking no prescription medication, stimulated parotid fluid output did not diminish with increased age. Of BLSA participants taking medication, post-menopausal women (but not older men) produced stimulated saliva at rates significantly lower than their non-medicated counterparts.

Baum BJ, Rousevelari EE, Oppenheim FG. Exocrine protein secretion from human parotid glands during aging: stable release of the acidic proline-rich proteins. J Gerontol 1982, 37:392-395.
Exocrine protein secretion from stimulated human parotid glands was examined using the anionic proline-rich proteins as a marker

for studying protein exocytosis. No differences were observed in the ability of BLSA women and men to secrete this group of exocrine secretory proteins with age.

Baum BJ, Bodner L. Aging and oral motor function: evidence for altered performance among older persons. J Dent Res 1983, 62:2-6.
Oral motor functions were evaluated in 257 BLSA women and men, ranging in age from 23-88 years. An increased prevalence of altered motor performance with age was found for parameters measuring lip posture and masticatory muscle function. Males, but not females, showed a higher prevalence of alterations in tongue function and in swallowing.

Baum BJ, Costa PT Jr, Isuzu KT. Sodium handling by aging human parotid glands is inconsistent with a two-stage secretion model. Am J Physiol 1984, 246:R35-R39.
Sodium handling by stimulated human parotid glands was evaluated in BLSA male and female participants across the adult life-span. Young adults secreted more sodium in the saliva than their middle-aged and older counterparts.

Baum BJ. Salivary gland function during aging. Gerodontics 1986, 2:61-64.
A critical review of available research data on salivary gland function during aging, concluding there is no generalieed diminution, with age, in salivary gland performance. Complaints suggestive of salivary gland disorders are more probably related to disease or therapy-induced perturbations.

Baum BJ. Age changes in salivary glands and salivary secretion. In: P Holm-Pedersen, H Loe, eds., Geriatric Dentistry - A Textbook of Oral Gerontology. Munksgaard, Copenhagen: 1986, 114-122.
Based on research indicating there is no generalieed diminution in salivary gland performance with increased age, clinicians must take care not to casually ascribe complaints, suggestive of salivary gland disorders, by older patients to aging, but rather to include age as one possibility in a differential diagnosis.

Baum BJ. Saliva secretion and composition. Front Oral Physiol 1987, 6:126-134.
A review of the scientific literature on salivary secretion and composition in aging. Although further research is needed, especially with submandibular and minor gland secretions, diminished salivary gland performance, once considered a fact of geriatric oral health, is better viewed as a myth.

Baum BJ. Salivary gland fluid secretion during aging. J Am Geriatr Soc 1989, 37:453-458.
Salivary gland function is generally well-preserved in healthy older males and females. Older people are, however, more likely to experience salivary disorders due to disease or its treatment.

For many patients with remaining salivary gland parenchymal tissue, improved function may be achieved with proper pharmacological therapy.

Baum BJ, Ship JA. The oral cavity. In: WR Hazzard, R Andres, EL Bierman, JP Blass, eds., Principles of Geriatric Medicine and Gerontology. New York: McGraw-Hill, 1990, 413-422.
This chapter focuses on specific oral tissues and their functions, presenting both what a clinician can reasonably expect to encounter as "normal" oral physiological status in the older male or female and the way common systemic disease and its treatment may affect the oral tissues during aging.

Baum BJ. Dental and oral disorders. In: WB Abrams, R Berkow, eds., The Merck Manual of Geriatrics. Rahway, NJ: Merck & Co., 1990, 466-475.
A review of the two major functions of the oral cavity (initiation of digestion and production of speech) and the oral diseases prevalent in older men and women. Most of these problems in older adults are not life-threatening but they may be serious, and many have a major impact on the quality of life.

Baum BJ, Caruso AJ, Ship JA, Wolff A. Oral physiology. In: T Papas, L Niessen, H Chauncey, eds., Geriatric Dentistry. St Louis: Mosby, (In Press).
Provides a current understanding of the general physiologic mechanisms involved in salivary gland secretion, motor/sensory performance; and the oral mucosal barrier with a review of what is known about their performance in the aging man or woman.

Baum BJ, Ship JA. Oral disorders. In: J Beck, et al., eds., American Geriatrics Society Geriatrics Review Syllabus. New York: AGS, (In Press).
In healthy women and men, BLSA and other research data indicate that many functions of oral tissues remain intact with age. Many systemic diseases and their treatment can influence oral tissue function, and the clinician should recognize that oral complaints and disorders in the elderly may not necessarily be a simple consequence of aging.

Fox PC, Heft MN, Herrera M, Bowers MR, Mandel ID, Baum BJ. Secretion of antimicrobial proteins from the parotid glands of different aged healthy persons. J Gerontol 1987, 42:466-469.
The secretion of three antimicrobial proteins from the parotid glands of 82 generally healthy BLSA men and women, 22-81 years old, was examined. The results are consistent with a maintenance of protective functions in parotid saliva during aging.

Heft MW. Prevalence of TMJ signs and symptoms in the elderly. Gerodontology 1984, 3:125-130.
The majority of reports profiling patients with signs and symptoms of temporomandibular joint (TMJ) disorders suggest most are

females (80%) in the 20-40 year age group. The only age differenae noted in an assessment of the prevalence of the signs and symptoms of TMJ disorders in BLSA participants was in limitation of jaw opening among the older subjects.

Heft MW, Baum BJ. Unstimulated and stimulated parotid salivary flow rate in individuals of different ages. J Dent Res 1984, 63: 1182-1186.
Both unstimulated and stimulated parotid saliva samples were oolleated from 85 healthy, unmedicated BLSA males and females between the ages of 23 and 81 years. There were no significant differences in flow rate related to age.

Scott J, Baum BJ. Oral effects of aging. In: JH Jones, DK Mason, eds., Oral Manifestations of Systemic Diseases. London: Bailliere Tindall, 1990, 311-338.
There exist certain age-related changes in oral structures and functions which may not be debilitating, especially in the healthy, older adult. However, such alterations may put the older person at risk in stressful or compromising conditions.

Ship JA, Baum BJ. Is reduced salivary flow normal in old people? Lancet, (In Press).
In the first reported longitudinal study of salivary gland function in humans, stimulated parotid gland flow rates over a 10 year period in predominantly healthy, different-aged BLSA women and men were investigated. No age- or sex-related changes over the 10 year period were observed.

Ship JA, Patton LL, Tylenda CA. An assessment of salivary output in healthy premenopausal and postmenopausal females. J Gerontol: Medical Sciences, (In Press).
The effects of menopausal status and estrogen therapy on subjective reports or oral dryness and discomfort and objective measurements of major salivary gland output were assessed in healthy BLSA premenopausal and postmenopausal women. No complaints of oral dryness or burning mouth and no alterations in the quantity of saliva occurred. This study suggests that among healthy women salivary gland function is not significantly influenced by menopause or hormonal replacement therapy.

Sonies BC, Baum BJ, Shawker TH. Tongue motion in elderly adults: initial in situ observations. J Gerontol 1984, 39:279-283.
Ultrasound was used to compare tongue motion at rest and during speech production and resting tongue thickness in normal older and younger men and women. Differences in direction and extent of tongue displacement were significant between young and old adults during production of one sound but not two others. Older persons showed a significant diminution in tongue thickness during rest; however, no evidence that tongue function was affected was found.

Tylenda CA, Ship JA, Fox PC, Baum BJ. Evaluation of submandibular salivary flow rate in different age groups. J Dent Res 1988, 67:1225-1228.
The production of unstimulated and citrate-stimulated submandibular saliva was examined in 90 BLSA men and women, aged 26-93 years. There was no diminution in submandibular gland fluid output, at rest or during stimulation, with increasing age. The results demonstrate that major gland fluid secretion capacity is maintained in healthy older individuals.

Wolff A, Ship JA, Tylenda CA, Fox PC, Baum BJ. Oral mucosal appearance is unchanged in healthy, different aged individuals. Oral Surg Oral Med Oral Path, (In Press).
Oral mucosal status was assessed in 94 BLSA men and 88 BLSA women, between 20 and 95 years old, according to both subjective complaints and a semiquantitative clinical rating scale. No changes in either criterion were detected with increasing age.

Smoking

Fozard JL, Pearson JD. Secular trends and cohort differences in smoking in the Baltimore Longitudinal Study of Aging. The Gerontologist 1990, 30:3A, (Abstract).
There is a striking decline over time in the prevalence of cigarette smoking among BLSA women and men of all ages.

Sex Differences in Brain Metabolism and Structure

Miura SA, Schapiro MB, Grady CL, Kumar A, Kozachuk WE, Wagner E, Rapoport SI, Horwitz B. The effect of gender on glucose utilization rates in healthy humans: a positron emission tomography study. J Neurosci Research, (In Press).
Positron emission tomography was used to see if sex differences in resting regional cerebral glucose utilization could be detected. A comparison of healthy young (age range: 21-38 years) non-BLSA women and men showed no significant differences in absolute global or regional glucose metabolism.

Azari NP, Schapiro MB, Rapoport SI, Horwitz B. Gender differences in correlations of cerebral glucose metabolic rates in young normal adults. J Cerebral Blood Flow and Metabolism, (Abstract).
A new correlation method was used to look at interrelations between pairs of metabolic rates in different brain regions of healthy non-BLSA men and women aged 18-40 years old, who were scanned with positron emission tomography under conditions of reduced auditory and visual stimulation. A significant sex difference was found with women having more correlated brain activity in the left hemisphere than men.

Creasy H, Schwartz M, Frederickson H, Haxby JV, Rapoport SI. Quantitative computed tomography in dementia of the Alzheimer type. Neurology 1986, 36:1563-1568.
In healthy non-BLSA men and women, quantitative computer assisted tomography of the brain demonstrated sex differences with regard to intracranial and cerebrospinal fluid volumes and in the volumes of the lateral cerebral ventricles. The computer assisted method to quantify the volumes of individual brain structures in brain CT scans and used in this study is described in:
DeLeo JM, Schwartz M, Creasey H, Cutler N, Rapoport SI. Computer-assisted categorization of brain computerized tomography pixels into cerebrospinal fulid, white matter and gray matter. Computers and Biomedical Research 1985, 19:79-88.

Sensation and Perception

Women's Perception: Two critical reviews of the current research literature have been published on vision, hearing, taste and smell. These reviews identify major research advances in the past decade, outline an agenda of research for the future, and lay the theoretical groundwork for various interventions to minimize the negative impact of aging on sensory function:

Schieber F, Fozard JL, Gordon-Salant S, Weiffenbach JM. Optimizing sensation and perception in older adults. International Journal of Industrial Erogonomics, (In Press).

Fozard JL. Vision and hearing in aging. In: Birren JE, Schaie, eds., The Handbook of the Psychology of Aging (3rd edition). New York: Academic Press, 1990, 150-170.

Vision: The first three of the following publications indicate that age related declines in visual function occur in both men and women independently of age related diseases of the eye and that environmental interventions are possible to compensate for the losses in function. The second two papers relate attempts of BLSA scientists to identify long-term risk factors for cataracts and macular disease:

Kline DW, Kline TJB, Fozard JL, Kosnik W, Schieber F, Sekuler R. Vision, aging and driving: the problems of older drivers. J Gerontol: Psycho1 Sci 1990, (In Press).

Gittings NS, Fozard JL. Age related changes in visual acuity. Exp Gerontol 1986, 21: 423-433.

Schieber F, Fozard JL, Dent CL, Kline D. Age and contrast sensitivity. Presented at the 42nd Annual Scientific Meeting of the Gerontological Society of America, Minneapolis, November 17-21, 1989.

Mele L, Alston C, Moorman C, Wang F, Fozard JL, Taylor HR, West S. Cataracts and cardiovascular disease. Presented at the 1990 ARVO Meeting, Sarasota, FL, April 29-May 2, 1990.

Vitale S, West S, Hallfrisch J, Alston C, Muller D. Nutritional status and risk of cataracts. To be presented at the Third National Eye Institute Symposium on Eye Disease and Epidemiology.

Hearincr: Increases in hearing thresholds occur with age in both women and men, but the amount of loss is less in women. Reaction times to auditory signals, both when decisions are required and when they are not, increase with age, more so in women than in men:

Brant LJ, Fozard JL. Age changes in pure-tone hearing thresholds in a longitudinal study of normal human aging. J Acoust Soc Am 1990, 88: 813-820.

Brant LJ, Morrell CH. Models for examining longitudinal changes in hearing threshold. J Am Stat Assn 1989, (In Press).

Fozard JL, Vercruyssen M, Reynolds SL, Hancock PA. Longitudinal analysis of age-related slowing: BLSA reaction time data. Santa Monica, CA: Human Factors Society, Proceedings of the 34th Annual Meeting 1990, 163-167.

Oral Bensory Function (BLSA and National Institute of Dental Research Collaboration)

Tylenda CA, Baum BJ. Oral physiology and the Baltimore Longitudinal Study of Aging. Gerodontology 1988, 7:5-9.
Since initiation of the oral physiology component of the BLBA in 1978 almost 500 women and men have been examined. Oral sensory skill deficits were found to be generally independent of age: olfactory ability, as measured by an olfactory recognition test, declined after age 65 for both sexes, as did the ability of older subjects to judge pressure differences applied to the tongue.

Bartoshuk LM, Weiffenbach JM. Chemical senses and aging. In: EL Schneider, JW Rowe, eds., Handbook of the Biology of Aging. San Diego: Academic Press, Inc, 1990, 429-443.
A review of available scientific data on the chemical senses and age. bubtle taste changes associated with aging have little impact on real-world taste experience. However, odors become less intense and harder to identify with age.

Weiffenbach JM, Baum BJ, Burghauser R. Taste thresholds: quality specific variation with human aging. J Gerontol 1982, 37:372-377.
Detection thresholds for each of the four basic taste qualities were obtained from BLBA women and men between 23 and 88 years of

age. Detection thresholds for the four taste qualities undergo different ohanges with age: citric acid alone shows a sex effect.

Weiffenbach JM. Taste and smell perception in aging. Gerodontology 1984, 3:137-144.
Our understanding of age-related changes in the perception of taste and smell is derived from inferences based on verbal reports and on the performance of tasks involving taste and smell stimuli. The perceptual disadvantage of older adults appears to be more marked or more easily measured for complex than for simple stimuli.

Weiffenbach JM, Cowart BJ, Baum BJ. Taste intensity perception in aging. J Gerontol 1986, 41:460-468.
In a study of 91 BLSA men and 79 BLSA women, significant age-related changes in taste intensity perception were demonstrated.

Weiffenbach JM, Fox PC, Baum BJ. Taste and salivary function. Proc Natl Acad Sci USA 1986, 83:6103-6106.
Taste perception was remarkably unimpaired in women with severe, chronic failure of all major and minor salivary gland function, demonstrating that the functional integrity of the taste system is not dependent upon the presence of normal saliva in the mouth.

Weiffenbach JM. Taste perception mechanisms. Front Oral Physiol 1987, 6:151-167.
Age-related changes in taste perception are not uniform for all taste qualities nor for all taste performances.

Weiffenbach JM. Taste changes with aging. Int J Tech Aging 1988, 1: 136-145.
A review of research using objective measures to study taste changes in aging.

Weiffenbach JM. Assessment of chemosensory functioning in aging: subjective and objective procedures. Ann NY Acad Sciences 1989, 561: 56-64.
Describes use of subjective and objective measures to assess sensory and perceptual functioning in aging.

Weiffenbach JM, Tylenda CA, Baum BJ. Oral sensory changes in aging. J Gerontol: Medical Sciences 1990, 45: M121-M125.
Perception of oral sensory intensity was assessed in BLSA women and men. Age had no significant effect on any of the response measures for any stimulus type except pressure. All measures of response to lingual pressure except median size declined significantly with age.

Cell Replication

Monticone R, O'Connor F, Gittings N, Waclawiw M, Brock M, Lakatta E, Fozard J, Eichhorn G, Schneider E. The effect of donor age on

the estimated in vitro lifespan of skin fibroblast cultures initiated from members of the Baltimore Longitudinal Study of Aging (BLSA). Presented at the 42nd Annual Scientific Meeting of the Gerontological Society of America, Minneapolis, November 17-21, 1989.
A significant decline in the estimated in vitro lifespan of cultured fibroblasts, derived from skin biopsies of BLSA mea and women, was observed from mea and women donors between ages 20-29 and later decades.

Persoaality, Stress and Coping, and Women's Health and Well-Being

Women's Personality Structure and Aging: BLSA research has contributed to the current consensus that personality in both mea and women can be described in terms of five basia faotors, and both longitudinal and cross-sectional studies have shown stability of these personality traits from early adulthood through advanced old age. In one BLSA study, 193 women, initially aged 23 to 86, were administered the Guilford-Zimmerman Temperament Survey, 8 measure of 10 personality traits. When readminisited the same instrument 4 to 10 years later, they showed no change in average level. Thus, stereotypes that portray aging women as becoming increasingly depressed, withdrawn, rigid, cranky, or apathetic are without empirical foundation. Further, individuals maintain their distinctive characteristics as they age: the young extravert becomes the old extravert, and the conservative older women was probably just as conservative in her youth. These studies and findings are described in the following publications.

McCrae RR. Consensual validation of personality traits: evidence from self-reports and ratings. J Personal and Soc Psycho1 1982, 43:293-303.

McCrae RR, Costa PT Jr. Self-concept and the stability of personality: cross-sectional comparisons of self-reports and ratings. J Personal and Soc Psycho1 1982, 43:1282-1292.

Costa PT Jr, McCrae RR, Arenberg D. Recent longitudinal research on personality and aging. In: KW Schaie, ed., Longitudinal Studies of Adult Development. New York: Guilford Press, 1983, 222-265.

McCrae RR, Costa PT Jr. Joint factors in self-reports and ratings: neuroticism, extraversion, and openness to experience. Personal and Indiv Differences 1983, 38:245-255.

McCrae RR, Costa PT Jr. Social desirability scales: more substance than style. J Consulting and Clin Psycho1 1983, 51: 882-888.

Costa PT Jr, McCrae RR. Concurrent validation after 20 years: the implications Of personality stability for its assessment. In:

JN Butcher, C Spielberger, eds., Advances in Personality Assessment, Vol. 4. Hillsdale, NJ: Lawrence Earlbaum, 1984, 31-54.

Costa PT Jr, McCrae RR, Holland JL. Personality and vocational interests in an adult sample. J Applied Psycho1 1984, 69:390-400.

McCrae RR, Costa PT Jr. Personality, stress, and coping processes in aging men and women. In: R Andres, E Bierman, W Hazzard, eds., Principles of Geriatric Medicine. New York: McGraw-Hill, 1985, 141-150.

McCrae RR, Costa PT Jr. Comparison of EPI and psychoticism scales with measures of the five factor model of personality. Personal Indiv Differences 1985, 6:587-597.

Costa PT Jr, Zonderman AB, McCrae RR, Williams RB. Content and comprehensiveness in the MMPI: an item factor analysis in a normal adult sample. J Personal Soc Psycho1 1985, 48:925-933.

McCrae RR, Costa PT Jr. Openness to experience. In: R Hogan, W Jones, eds., Perspectives in Personality: Theory, Measurement, and Interpersonal Dynamics, Vol. 1. Greenwich, CT: JAI Press, 1985, 145-172.

McCrae RR, Costa PT Jr. Updating Norman's adequate taxonomy of personality: personality dimensions in intelligence and personality. J Personal Soc Psycho1 1985, 49:710-721.

Costa PT Jr, Busch CM, Zonderman AB, McCrae RR. Correlations of MMPI factor scales with measures of the five factor model. J Personal Assessment 1986, 50:640-650.

Costa PT Jr, McCrae RR. Major contributions to the psychology of personality. In: S and C Modgil, eds., Hans Eysenck: Searching for a Scientific Basis for Human Behavior. Barcombe Lewes Sussex, England: Falmer, 1986, 63-72, 86-87.

McCrae RR. Well-being scales do not measure social desirability. J Gerontology 1986, 41:390-392.

McCrae RR, Costa PT Jr, Busch CM. Evaluating comprehensiveness in personality systems: The California Q-Set and the five factor model. J Personality 1986, 54:430-446.

Costa PT Jr, McCrae RR. Age, personality, and the Holtzman Inkblot Technique. Inter J Aging and Human Devel 1986, 23: 133-143.

Costa PT Jr, McCrae RR. Cross-sectional studies of personality in a national sample: I. development of survey measures. Psycho1 and Aging 1986, 1:140-143.

Costa PT Jr, McCrae RR, Zonderman AB, Barbano HE, Lebowitz B, Larson DM. Cross-sectional studies of personality in a national sample: II. stability in neuroticism, extraversion, and openness. Psycho1 and Aging 1986, **1:144-149.**

Costa PT Jr, McCrae RR. The case for personality stability. In: GL Maddox, EW Busse, eds., Aging: The Universal Human Experience. Selected papers from the symposia **of** the **XIIIth** Congress of the International Association of Gerontology. New York: Springer, 1987.

McCrae RR. Creativity, divergent thinking, and openness to experience. J Personal **Soc** Psycho1 1987, **52:1258-1265.**

McCrae RR, Costa PT Jr. Validation of the five factor model of personality across instruments and observers. **J** Personal **Soc** Psycho1 1987, **52:81-90.**

Costa PT Jr, McCrae RR. From catalog to classification: Murray's needs and the five-factor model. **J** Personal **Soc** Psycho1 1988, 55: 258-265.

McCrae RR, Costa PT Jr. Recalled parent-child relations and adult personality. **J** Personality 1988, **56:417-434.**

Costa PT Jr, McCrae RR. Personality in adulthood: a six-year longitudinal study of self-reports and spouse ratings of the NEO-PI. **J** Personal **Soc** Psycho1 1988, **54:853-863.**

McCrae RR, Costa PT Jr. Age, personality, and the spontaneous self-concept. J Gerontol: Social Sciences 1988, **43:S177-S185.**

Costa PT Jr, McCrae RR. Personality continuity and the changes of adult life. In: M Storandt, GR **VandenBos,** eds., The Adult Years: Continuity and Change. Washington, DC: **APA,** 1989, 45-77.

McCrae RR. Why I advocate the five-factor model: joint analyses of the NEO-PI and other instruments. In: DM Buss, N Cantor, eds., Personality Psychology: Recent Trends and Emerging Directions. New York: Springer-Verlag, 1989, 237-245.

McCrae RR, Costa PT Jr. Different points of view: self-reports and ratings in the assessment of personality. In: JP **Forgas** and **MJ** Innes, eds., Recent Advances in Social Psychology: An International Perspective. Amsterdam: Elsevier Science, 1989, 429-439.

McCrae RR, Costa PT Jr. Reinterpreting the Myers-Briggs Type Indicator from the perspective of the five-factor model of personality. **J** Personality 1989, **57:17-40.**

McCrae RR, Costa PT Jr. Rotation to maximize the construct validity of factors in the NEO Personality Inventory. Multivariate Behav Res 1989, 24:107-124.

McCrae RR, Costa PT Jr. The structure of interpersonal traits: Wiggins' circumplex and the five-factor model. J Personal Soc Psycho1 1989, 56:586-595.

McCrae RR. Trait's and trait names: how well is openness represented in natural languages? European J Personal 1990, 4: 119-129.

McCrae RR, Costa PT Jr. Personality in Adulthood. New York: Guilford, 1990.

Costa PT Jr, McCrae RR. Longitudinal stability of adult personality. In: SR Briggs, R Hogan, NH Jones, eds., Handbook of Personality Psychology. New York: Academic Press, (In Press).

Costa PT Jr, McCrae RR. Multiple uses for longitudinal personality data. European J Personal, (In Press).

Costa PT Jr, McCrae, RR. The NEO Personality Inventory (NEO-PI). In: SR Briggs, J Cheek, eds., Personality Measures, Vol. 1. Greenwich, CT: JAI Press, (In Press).

McCrae RR, Costa PT Jr. Conceptions and correlates of Openness to Experience. In: SR Briggs, R Hogan, NH Jones, eds., Handbook of Personality Psychology. New York: Academic Press, (In Press).

McCrae RR, John OP. An introduction to the five-factor model and its applications. In: RR McCrae, ed., The Five-Factor Model: Issues and Applications [Special Issue]. J Personal, (In Press).

Piedmont RL, McCrae RR, Costa PT Jr. Adjective check list scales and the five-factor model. J Personal Soc Psychol, (In Press).

Piedmont RL, McCrae RR, Costa PT Jr. An assessment of the EPPS from the perspective of the five-factor model. Psychological Assessment: J Consulting and Clin Psychol, (In Press).

Stress and Women's Coping Mechanisms; There are many possible ways to deal with stress, from taking direct action to solve the problem to reliance on positive thinking. Studies on BLSA women have shown that the choice of coping mechanisms is a function both of enduring personality traits and of the requirements and. opportunities of the particular situation. For example, women who are extraverted are more likely than introverted women to use positive thinking in response to a stressor; women who have suffered a loss are more likely to be fatalistic than women who face a difficult but challenging task. Other studies have shown that most women are capable of coping with one of the most severe

stressors, bereavement. Relevant publications by BLSA investigators are:

McCrae RR. Are stress questionnaires stressful? IRB: A Review of Human Subjects Research 1981, 4:1-2.

McCrae RR. Age differences in the use of coping mechanisms. J Gerontology 1982, 37:454-460.

McCrae RR. Situational determinants of coping responses: loss, threat, and challenge. J Personal Soc Psycho1 1984, 46:919-928.

Schroeder DH, Costa PT Jr. The influence of life event stress on physical illness: substantive effects or methodological flaws? J. Personal Soc Psycho1 1984, 46:853-863.

McCrae RR, Costa PT Jr. Personality, coping and coping effectiveness in an adult sample. J Personal 1986, 54:385-405.

McCrae RR, Costa PT Jr. Psychological resilience among widowed men and women: a lo-year followup of a national sample. J Soc Issues 1988, 44:129-142.

McCrae RR. Age differences and changes in the use of coping mechanisms. J Gerontology: Psychological Sciences 1989, 44: P161-P169.

Costa PT Jr, McCrae RR. Personality, stress, and coping: some lessons from a decade of research. In: KS Markides, CS Cooper, eds., Aging, Stress and Health. New York: Wiley 1989, 267-283.

Costa PT Jr, Zonderman AB, McCrae RR. Personality, defense, coping, and adaptation in older adulthood. In: EM Cummings, AL Greene, KH Rarraker, eds., Lifespan Developmental Psychology, Vol. 11: Perspectives on Stress and Coping. Hillsdale, NJ: Lawrence Erlbaum 1990, 277-293.

McCrae RR. Situational determinants of coping. In: BN Carpenter, ed., Personal Coping: Theory, Research and Applications. New York: Praeger (In Press).

Personality and Women's Health: Psychosomatic medicine is the study of psychological influences on physical health. Research by BLSA investigators has pointed out the need to distinguish somatic complaints from actual illness. In a study of 345 women who completed the Cornell Medical Index, the total number of physical complaints was strongly correlated with the number of psychiatric complaints. Physical complaints were also associated with peer ratings of these women on the personality dimension of Neruroticism vs. Emotional Stability. Other studies suggest that this is not because psychological maladjustment leads to disease, but rather because maladjustment increases the perception, recall,

and reporting of medical complaints. Neuroticism (On8 of the domains in the five-factor model of personality applicable to both men and women) is thus a factor that should be considered in evaluating the validity of self-reports of health. Publications by BLSA scientists in this research area are:

Costa PT Jr, Zonderman AB, **McCrae** RR, Williams RB. Cynicism and paranoid alienation in the Cook and Medley HO scale. Psychosomatic **Med** 1986, **48:283-285.**

Whitehead WE, Busch CM, **Heller** BR, Costa **PT** Jr. Social learning influences on menstrual symptoms and illness behavior. Health Psycho1 1986, **5:13-23.**

Zonderman AB, Leu VL, Costa PT Jr. Effects of age, hypertension history, and neuroticism on **health** perceptions. **Exper Gerontol** 1986, **21:449-458.**

Costa PT Jr, McCrae RR. Neuroticism, somatic complaints and disease: is the bark worse than the bite?' **J** Personality 1987, 55: 299-316.

Costa PT Jr, McCrae RR. Personality assessment in psychosomatic medicine: value of a trait taxonomy. In: GA Fava, TN Wise, eds., Advances in Psychosomatic Medicine, Vol. 17. Research Paradigms in Psychosomatic Medicine. Basel: Rarger 1987, 71-82.

Busch CM, Costa PT Jr, Whitehead WE, Heller BR. Severe perimenstrual symptoms: prevalence and effects on absenteeism and health care seeking in a non-clinical sample. Women **&** Health 1988, **14:59-74.**

Whitehead WE, Bosmajian L, Zonderman AB, Costa PT Jr, Schuster MM. Symptoms of psychologic distress associated with irritable bowel syndrome: comparison of community and medical clinic samples. Gastroenterology 1988, **95:709-714.**

Costa PT Jr, McCrae RR, Dembroski TM. Agreeableness vs. antagonism: explication of a potential risk factor for CHD. In: A Siegman, TM Dembroski, eds., In Search of Coronary-Prone Behavior: Beyond Type A. Hillsdale, NJ: Erlbaum Associates, 1989, 41-63.

McCrae RR, Costa PT Jr, Dahlstrom WG, Barefoot JC, Siegler IC, Williams RB Jr. A caution on the use of the MMPI K-correction in research on psychosomatic medicine. Psychosomatic Med 1989, **51:58-65.**

Zonderman AB, Costa PT Jr, McCrae RR. Depression as a risk factor for cancer morbidity and mortality in a nationally representative sample. **JAMA** 1989, **262:1191-1195.**

Costa PT Jr, Zonderman AB, McCrae RR. Cancer and psychosocial traits, continued [Letter to the Editor]. JAMA 1990, 263:514.

Stone SV, Dembroski TM, Costa PT, Jr, MacDougall JM. Gender differences in cardiovascular reactivity. J Behav Med 1990, 13: 137-156.

Whitehead WE, Crowell MD, Bosmajian L, Zonderman AB, Costa PT, Benjamin C, Robinson JC, Heller BR, Schuster MM. Existence of irritable bowel syndrome supported by factor analysis of symptoms in two community samples. Gastroenterology (In Press).

Siegler IC, Zonderman AB, Barefoot J, Williams RB Jr, Costa PT Jr, McCrae RR. Predicting personality in adulthood from college MMPI scores: implications for follow-up studies in psychosomatic medicine. Psychosomatic Med (In Press).

Women's Psychoolooical Health and Well-beinq: A number of studies have examined relations between enduring personality dispositions and psychological health and well-being. In general, women who are emotionally stable, extraverted, agreeable, and conscientious have higher levels of happiness and life satisfaction.n. Further, personality traits are related to some categories of psychiatric disorders. For example, women who are very introverted are more likely to score high on measures of Schizoid Personality Disorder. Such findings are useful to counselors, clinical psychologists, and psychiatrists who can use information on personality traits to understand their patients, select appropriate therapies, and anticipate the course of therapy. This research contributes to the psychological health of aging women and is described in the following publications.

McCrae RR. Extraversion is not a filter, neuroticism is not an outcome: a reply to Lawton. Exper Aging Res 1983, 9:73-76.

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